

The Journal of Obstetrics and Gynaecology of the British Empire

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EARLY AMBULATION

Suture tensile strength and elasticity are of great importance
to surgeons who practice the new procedure.

LONDON HOSPITAL ULTRATAN CATG
(MORLEY'S PROCESS)

HAS AN AVERAGE TENSILE STRENGTH

28% greater than B.P.C. requirements

and

19% greater than U.S.A. requirements

(This average is struck from numerous tests before release)

ELASTICITY

The elongation (elasticity) of London Hospital Ultratan Catg.
giving the necessary expansion to

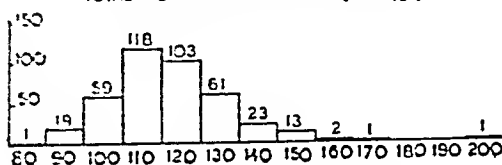
THE LONDON HOSPITAL

FREQUENCY DISTRIBUTION OF BLOOD PRESSURE

AGE GROUP 20-29

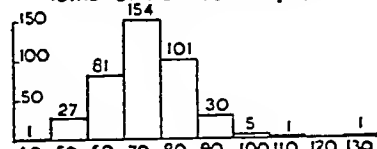
Nulliparae 20-29 Systolic B.P.

TOTAL 401 MEAN 119.28 mmHg S.D. 15.7



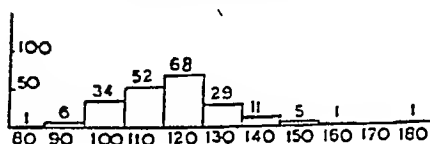
Nulliparae 20-29 Diastolic B.P.

TOTAL 401 MEAN 76.2 mmHg S.D. 11.3



Multiparae 20-29 Systolic B.P.

TOTAL 208 MEAN 121.8 mmHg S.D. 14.1



Multiparae 20-29 Diastolic B.P.

TOTAL 208 MEAN 77.4 mmHg S.D. 10.8

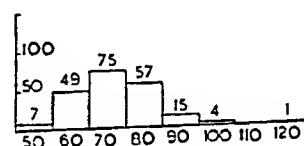


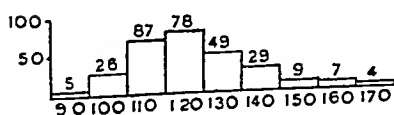
Figure 2

FREQUENCY DISTRIBUTION OF BLOOD PRESSURE

AGE GROUP 30-39

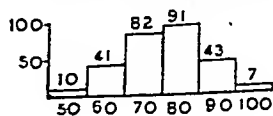
Nulliparae 30-39 Systolic B.P.

TOTAL 274 MEAN 126.9 mmHg S.D. 15.5



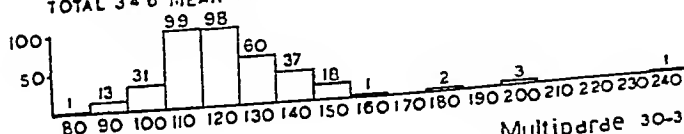
Nulliparae 30-39 Diastolic B.P.

TOTAL 274 MEAN 78.5 mmHg S.D. 12.3



Multiparae 30-39 Systolic B.P.

TOTAL 346 MEAN 126.0 mmHg S.D. 15.0



Multiparae 30-39 Diastolic B.P.

TOTAL 384 MEAN 79.0 mmHg S.D. 13.2

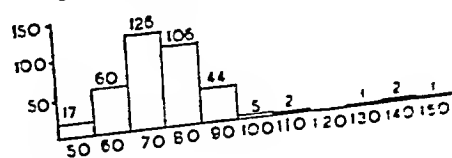


Figure 3

FREQUENCY DISTRIBUTION OF BLOOD PRESSURE

AGE GROUP 40-49.

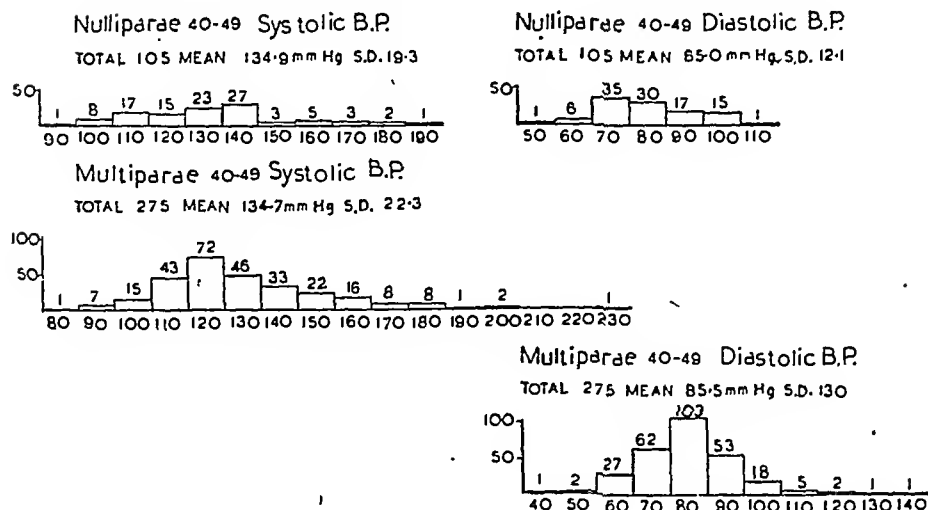


Figure 4.

FREQUENCY DISTRIBUTION OF BLOOD PRESSURE

AGE GROUP OVER 50

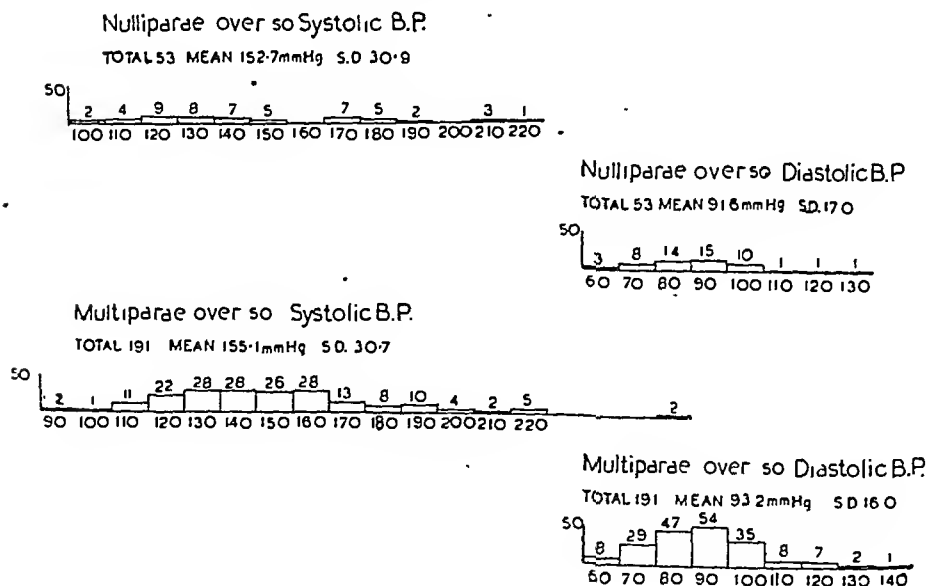


Figure 5

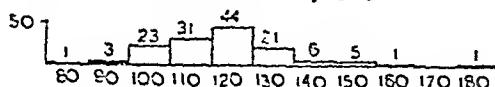
BLOOD-PRESSURE AND THE INCIDENCE OF HYPERTENSION

EFFECT OF PARITY ON BLOOD PRESSURE

MULTIPARAE 20-29 TOTAL 208

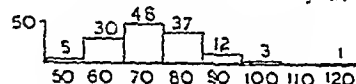
Para 1 Systolic B.P.

TOTAL 136 MEAN 119.4 mm Hg S.D. 13.5



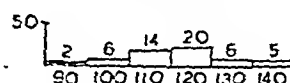
Para 1 Diastolic B.P.

TOTAL 136 MEAN 77.6 mm Hg S.D. 11.4



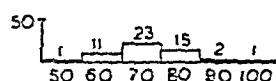
Para 2 Systolic B.P.

TOTAL 53 MEAN 122.0 S.D. 13.5



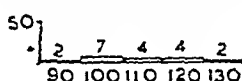
Para 2 Diastolic B.P.

TOTAL 53 MEAN 76.7 mm Hg S.D. 2.9



Para 3 and more Systolic B.P.

TOTAL 19 MEAN 113.5 mm Hg S.D. 10.8



Para 3 and more Diastolic B.P.

TOTAL 19 MEAN 76.8 mm Hg S.D. 9.5

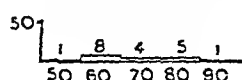


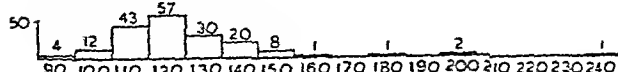
Figure 6.

EFFECT OF PARITY ON BLOOD PRESSURE

MULTIPARAE 30-39 TOTAL 364

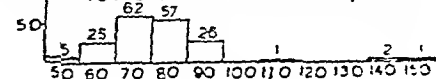
Para 1 Systolic B.P.

TOTAL 179 MEAN 128.0 mm Hg S.D. 18.5



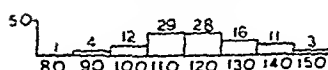
Para 1 Diastolic B.P.

TOTAL 179 MEAN 80.6 mm Hg S.D. 13.5



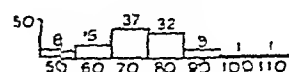
Para 2 Systolic B.P.

TOTAL 104 MEAN 123.1 mm Hg S.D. 14.0



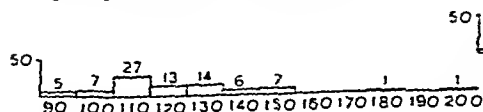
Para 2 Diastolic B.P.

TOTAL 104 MEAN 77.5 mm Hg S.D. 10.6



Para 3 and more Systolic B.P.

TOTAL 81 MEAN 127.7 mm Hg S.D. 18.5



Para 3 and more Diastolic B.P.

TOTAL 81 MEAN 78.2 mm Hg S.D. 14.0

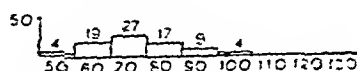


Figure 7.

EFFECT OF PARITY ON BLOOD PRESSURE.

MULTIPARAE 40-49

TOTAL 275

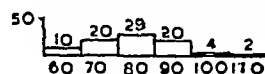
Para 1 Systolic B.P.

TOTAL 85 MEAN 133.0 mm Hg S.D. 19.0



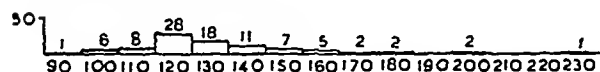
Para 1 Diastolic B.P.

TOTAL 85 MEAN 85.1 mm Hg S.D. 11.2



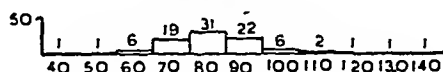
Para 2 Systolic B.P.

TOTAL 91 MEAN 137.9 mm Hg S.D. 22.6



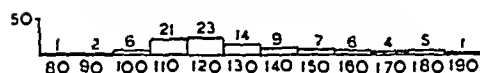
Para 2 Diastolic B.P.

TOTAL 91 MEAN 86.9 mm Hg S.D. 14.9



Para 3 and more Systolic B.P.

TOTAL 99 MEAN 133.2 mm Hg S.D. 23.3



Para 3 and more Diastolic B.P.

TOTAL 99 MEAN 86.4 mm Hg S.D. 11.9

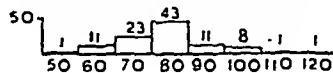


Figure 8.

Renal Failure in Obstetric Practice

BY

G. SHEDDEN ADAM, M.B., B.S., F.R.C.S., M.R.C.O.G.

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RECENT contributions to medical literature have, in many instances, related directly or indirectly to the problem of renal failure.

It may be timely, therefore, briefly to review the whole question of renal failure as encountered in obstetric practice, to apply our knowledge of renal physiology and of diuretic substances to this problem, to record certain illustrative case histories and to indicate such methods of treatment as have been found of value.

Partial or complete suppression of urine may develop as a complication of pregnancy or the puerperium from a variety of causes. It is a recognized, though not a particularly frequent, complication of eclampsia and, of course, is likely to develop in the less frequently encountered acute glomerulonephritis when this occurs during pregnancy or the puerperium.

Renal failure may follow a transfusion reaction resulting from an unrecognized Rh-incompatibility, and it is now apparent that pregnant and puerperal women are especially liable to be involved in such reactions.

Quite apart from the transient oliguria of obstetric shock, there is evidence that urinary suppression may develop as the result of maternal birth trauma, and the pathological and clinical features in these cases are said to have much in common with the "compression syndrome" as described in recent observations on air-raïd casualties.

The association of renal failure and concealed accidental haemorrhage is also re-

cognized. Symmetrical cortical necrosis of the kidneys, though rare, is another cause of severe and often fatal anuria, usually but not invariably associated with pregnancy, and preceded, in many cases, by a concealed accidental haemorrhage.

More remote possibilities are extensive renal infarction, bilateral ureteral obstruction and *Clostridium welchii* septicaemia.

RENAL PHYSIOLOGY.

Studies of renal physiology show that, although glomerular filtration is essential for urine formation, it is supplemented by tubular excretion of certain substances. Absorption, however, is the chief function of the renal tubules; water and various constituents of the body being reabsorbed from the glomerular filtrate if the plasma content of these constituents falls below a certain concentration; in other words urine is derived from blood plasma by the selective work of the kidney.

Clinically, urinary suppression is likely to develop (in the absence of circulating diuretic substances) if the systolic blood-pressure falls below 75 mm. Hg. because of the fall in hydrostatic pressure in the glomerular capillaries. This is no longer sufficient to overcome the osmotic pressure exerted by the plasma-proteins and the resistance offered by capsular pressure.

The plasma osmotic pressure has been estimated as approximately 30 mm. Hg. and the capsular pressure as approximately

15 mm. Hg., so that the effective hydrostatic pressure within the glomerular capillaries must exceed 45 mm. Hg. for filtration to occur.

Within certain limits any change in the arterial pressure will be reflected in an altered filtration pressure and, therefore, in the rate of filtration. Nevertheless, while a marked fall in blood-pressure usually results in a diminution or suppression of urine, an increased arterial pressure is not necessarily accompanied by an increased output.

Reduction in effective glomerular filtration to the point of urinary suppression also occurs when the pressure within the ureter is raised to about 30 mm. Hg. above atmospheric pressure.

Determination of the rate of urine excretion is normally affected primarily by regulation of the fraction of water reabsorbed by the tubules, rather than by regulation of the filtration rate itself. This concentration of the glomerular filtrate is, at least in part, controlled by the anti-diuretic hormone of the posterior pituitary lobe which, passing into the bloodstream, acts by accelerating the reabsorption of water from the tubular urine.

The study of diuretic substances and their effect on renal physiology is obviously important in considering the management of renal failure as encountered in obstetric practice. The simplest form of diuresis is that which follows the ingestion or parenteral administration of sufficient water to produce a relatively abrupt blood dilution. The increased urinary output in these circumstances is considered to be due to the temporary inhibition of the secretion of the anti-diuretic pituitary hormone.

An increased urinary output may also be brought about by temporarily increasing the concentration of electrolytes in the blood. The majority of electrolytes occurring in normal plasma are threshold

substances inasmuch as they are retained in the body when the plasma level has fallen and are freely excreted when the plasma level is raised. The excretion of those electrolytes present in excess of the normal plasma levels is usually accompanied by a diuresis. Thus, while the ingestion of an isotonic sodium chloride solution is not followed by an increased urinary output, the parenteral administration of a hypertonic sodium chloride solution causes a marked diuresis in the normal subject.

Again, effective diuresis in healthy persons, and in some patients exhibiting an oliguria, may be obtained by the intravenous administration of substances such as sodium sulphate which are not, to any appreciable extent, reabsorbed by the tubular epithelium.

The increased urinary output in these circumstances is probably due to the interference with the reabsorption of water from the glomerular filtrate exerted by the osmotic pressure or ionic concentration of these substances.

Diuresis may also occur as the result of a sudden disturbance of the osmotic equilibrium of the plasma. This is the basis of the intravenous glucose (dextrose) therapy (using a 25 per cent or 30 per cent solution) used in the management of eclamptic patients.

Titus,¹ Deickmann² and others considered that, if more glucose could be introduced into the body over a short period of time than could be burned, stored as glycogen or polymerized, the excess would, theoretically, be excreted in the urine, resulting in a polyuria.

Effective diuresis was obtained in eclamptic patients by the intravenous administration of 1,000 c.c. of a 20 per cent glucose solution (200 gm.) over a period of 30 to 50 minutes, especially if the treatment were repeated in 8 to 12 hours' time.

Examination of urine collected over a

26 hours' period of such treatment, however, demonstrated that comparatively little or no glucose was excreted in the urine, but that there was a constant increase in the chloride excretion.

The explanation of this, it was suggested, lay in the fact that the osmotic equilibrium of the plasma could be restored more easily by the excretion of chlorides which exert a greater osmotic pressure than glucose; 1 grm. of sodium chloride exerting 5 times as much osmotic pressure as 1 grm. of glucose.

Reference will be made to this form of therapy in the case reports to be quoted.

ECLAMPSIA.

The excretion of water in the normal pregnant patient tends to be faulty, and in severe pre-eclampsia and eclampsia oliguria (excretion of less than 600 c.c. of urine in 24 hours) occurs in 75 per cent to 85 per cent of cases; anuria (absence of urine for 12 hours or more) occurs in 1 per cent to 3 per cent of cases.² Zangemeister, from his observations on urinary suppression in eclampsia and pre-eclampsia, considered that this was most marked during the convulsive stage and concluded that both the convulsions and the oliguria depended on the same cause. Spickman, on the other hand, formed the impression that the oliguria of eclamptic patients was especially common after delivery and was usually accompanied by a lowered blood-pressure.

Mortality statistics for eclampsia indicate that the death-rate is in the region of 44 per cent if the oliguria lasts for more than 24 hours, and 90 per cent if it persists in spite of treatment.² The significance of the fact that many of these cases do not die of uraemia (c.f. symmetrical cortical renal necrosis where the oliguria may persist for 8-12 days before death from uraemia occurs) will be considered subsequently.

There is reason to believe that spasm of the intrarenal arterioles with glomerular ischaemia is a more likely cause of the urinary suppression in eclampsia than simple oedema of the kidney. The glomerular lesion is peculiar to eclampsia and the changes described are not necessarily irreversible; although hyalinization of some glomeruli, due to complete obliteration of capillaries, undoubtedly occurs in some cases. The power of recovery of the glomeruli is evident in the spontaneous diuresis which usually follows the successful management of the eclamptic patient, and in the uneventful course of subsequent pregnancies in many instances.

While a spontaneous diuresis may be anticipated, such a development is by no means assured, and there is evidence that a therapeutically induced diuresis at any earlier stage may favourably influence the prognosis for reasons other than those directly related to the urinary output. A digression, therefore, from the consideration of actual renal failure may be permitted. If it be accepted that the convulsions, the coma, the tachycardia and pyrexia, and possibly the visual disturbances of eclampsia, are due to cerebral anoxaemia resulting from oedema of the brain, then any effective method of combating and reducing the cerebral oedema must inevitably reduce that element in the mortality resulting from repeated convulsive seizures, deep coma, exhaustion and cardiac failure. There is, of course, nothing intrinsically new in this conception; it is rather to the method of inducing a diuresis sufficient to relieve the cerebral oedema that attention has been directed in recent years.

The effective diuresis which will often follow the intravenous administration of hypertonic solutions of glucose in eclamptic patients has already been referred to. The greater degree of success which has been achieved with this measure in contrast to

that obtained by other diuretic or dehydrating agents may be due to the co-incidental excretion of abnormally retained chlorides. It is well known that chloride retention in eclampsia is an aggravating feature of the condition, being due, probably, to retention of sodium with resultant retention of chloride, rather than to failure of the kidneys to excrete chloride.

Dieckmann² found that the urine from eclamptic patients on admission was relatively low in chlorides but that, after a diuresis had been established, whether spontaneously following delivery or by the intravenous administration of hypertonic glucose solution, the concentration of sodium chloride increased despite the increased urinary output.

Our own experience in the use of this diuretic agent in the management of both pre-eclamptic and eclamptic patients has been encouraging. Originally reserved for those cases exhibiting a severe oliguria, it is now given as part of the routine treatment of eclampsia. Although it failed to alter the course of the fatal illness in 1 case of fulminating eclampsia, we have, on several occasions, felt it to be a life-saving procedure.

In the moderately severe case of eclampsia in which there has not been any grave risk to the mother's life nor anuria, the routine use of hypertonic glucose solutions intravenously has appeared to hasten the convalescence and to abolish almost entirely that mental retardation which so often delays complete recovery from the post-eclamptic state. It has proven especially useful in those eclamptic patients, usually but not necessarily manifesting an oliguria, in whom the convulsions have been brought under control and measures taken, often successfully, to induce labour, but in whom there is no lessening in the depth of their coma.

It has been our experience that, in all but

the milder cases, the intravenous administration of the hypertonic glucose solution has to be repeated, and in this connexion a urinary output averaging less than 30 c.c. per hour is regarded as an indication for repeating the treatment. The initial diuresis, while effective (600-900 c.c.) is often short-lived, whereas the improved urinary output which usually follows the second or third treatment tends to be maintained, probably because it coincides with a general recovery from the eclamptic state.

Judicious selection of available veins is necessary, commencing at the more distal sites on the limb. Thrombophlebitis around the point of cannula, so troublesome when glucose solutions are given by the slow drip technique, is obviated by the more rapid rate of infusion.

The following case report is illustrative of the response obtained in eclamptic patients:

CASE I.

Mrs. J. J., a previously healthy primipara, aged 20 years, was admitted to hospital at 6.15 a.m. on May 15th, 1944, as a case of intrapartum eclampsia.

The urine, on admission, was scanty (56 c.c. only obtained) and "solid" with albumin, the blood-pressure was 190/110 mm. Hg. and the patient was comatose and subject to frequent eclamptic convulsions.

Fortunately labour was well advanced and it was possible to deliver the patient of a living female infant 3 hours later. Nevertheless, the convulsions persisted, the coma deepened, and the pulse-rate rose to 136 beats per minute.

Hypertonic glucose (1,000 c.c. of a 25 per cent solution) was given by the intravenous route at 11.30 a.m. and 480 c.c. of urine were obtained by catheterization an hour later.

Convulsions ceased at 2.30 p.m. but the patient remained deeply comatose. In view of this fact a further 1,000 c.c. of 25 per cent glucose solution were given intravenously at 7.30 p.m. This was followed by a satisfactory diuresis (600 c.c.), but on the following day (May 16th) the urinary output

had fallen again to a critical level and the patient was still comatose, with a pulse-rate of 140 beats per minute, and a temperature of 104°F. The urine contained a "half" deposit of albumin.

Another 1,000 c.c. of 25 per cent glucose were therefore given intravenously and the urinary output again improved. The relative diuresis, moreover, was maintained on this occasion, the amount of urine secreted averaging just over 90 c.c. per hour and containing only a "deposit" of albumin.

In spite of this the patient was still comatose on the following day (May 17); this being the 3rd day of the coma, and the prognosis appeared gloomy. (Blood urea estimation 126 mg. per 100 c.c. blood.) However, towards evening the coma lightened, and the patient recognized and spoke to her husband.

From this time the clinical picture was one of steady improvement. Complete consciousness was present the following day (May 18th), the urinary output continued at a satisfactory level, the blood-pressure had fallen to 130/80 mm. Hg., the albumin had disappeared from the urine and the blood urea had fallen to 36 mg. per 100 c.c. of blood by May 20th. The patient and her baby were discharged from hospital in good health and spirits on the 21st day after admission.

This form of treatment may also be used with advantage in certain cases of pre-eclampsia with oliguria as illustrated by the following case record:

CASE 2.¹

Mrs. M. K., a multipara aged 37 years, was referred for hospital treatment on June 17th, 1944, when 39 weeks pregnant, because of the development of severe pre-eclamptic manifestations; headaches, gross oedema of the face, hands and ankles, a blood-pressure of 230/150 mm. Hg. and a "two-thirds" deposit of albumin in the urine, which had been diminished in volume. The patient was dyspnoeic and generally distressed.

Routine treatment was commenced, including the 6-hourly administration of ammonium chloride in 10 grain doses as a diuretic. Nevertheless, the urinary output for 24 hours ending at midnight on June 18th was only 614 c.c., and for the next 12 hours only 224 c.c. of urine were secreted. Hypertonic glucose was therefore given at 7.30 p.m.

(1,000 c.c. of a 25 per cent solution) intravenously, and 1,530 c.c. of urine were passed during the next 12 hours.

The patient gave birth to a living female infant at 6.15 a.m. on June 20th but, on catheterization 6 hours later, only 90 c.c. of urine were obtained, which was "solid" with albumin.

A further 1,000 c.c. of 25 per cent glucose solution were therefore given intravenously. This was followed by a satisfactory diuresis (1,110 c.c. of clear urine over a period of 1½ hours following the commencement of the intravenous therapy).

On June 21st the oedema was appreciably less, the urinary output was 1,950 c.c., and the blood-urea was 42 mg. per 100 c.c. blood. The blood-pressure, however, was 200/118 mm. Hg. and was still 190/110 mm. Hg. 2 weeks later.

In spite of the persistent hypertension (suggesting previous vascular disease) the marked improvement in the general appearance and demeanour of this woman was both rapid and striking.

That such improvement might well have occurred following delivery without specific treatment to establish a diuresis must be admitted, but the impression was formed that, in a patient verging so closely on the eclamptic state, recovery without convulsive phenomena had been facilitated by the hypertonic glucose therapy.

ACUTE GLOMERULONEPHRITIS.

Acute glomerulonephritis, *per se*, is an uncommon complication of pregnancy, and the incidence (including recurrent attacks), in a large series of cases recently reviewed,² was found to be as low as 0.05 per cent. If, however, acute nephrosis (or the nephrotic form of acute glomerulonephritis) is included, these conditions may resemble pre-eclampsia or even eclampsia to such an extent that at times the correct diagnosis cannot be made until after the confinement.

On the other hand, the contention that such differences as exist in the clinical and pathological manifestations of the acute

diseases of the kidney on the one hand, and the toxæmias of pregnancy on the other, are purely incidental to the pregnancy, has little to support it.

What, then, are the criteria necessary for a diagnosis of acute glomerulonephritis complicating pregnancy? A recent focal infection, often streptococcal, the persistence of red blood cells in the urine for a period longer than a week, nitrogen retention and the persistence of oedema and albuminuria after delivery indicate, in a previously healthy patient, that the condition is likely to be one of acute nephritis (possibly of the nephrotic type) rather than a simple pregnancy toxæmia.

Should the decision rest upon autopsy evidence, careful examination of sections from the kidney may be necessary. Endothelial proliferation in the glomeruli with leucocytic infiltration would favour acute glomerulonephritis.

While both conditions are comparatively rare, the diagnosis, on purely clinical grounds, between acute nephritis complicating pregnancy and symmetrical cortical necrosis of the kidneys may present difficulties. The latter condition, however, is characterized by the late development of uraemic manifestations (resembling surgical anuria), a transient haematuria and an associated accidental antepartum haemorrhage in many cases.

Acute glomerulonephritis must therefore be considered in the investigation of any obstetrical case exhibiting an oliguria or anuria not obviously due to other causes.

The following case history, for example, illustrates the difficulty in distinguishing the syndrome of pre-eclampsia from that of acute glomerulonephritis.

CASE 3.

Mrs. J. W. was a primipara, aged 19 years, who subsequently gave a history of recent attacks of tonsillitis. The pregnancy had been uneventful until the 30th week, when she made her 6th ante-

natal visit on August 3rd, 1942, complaining of swollen ankles and headaches. Her blood-pressure, previously 130/90 mm. Hg., had risen to 180/112 mm. Hg., and her urine, previously clear, showed a "seven-eighths deposit" of albumin. She was admitted to hospital as a case of pre-eclampsia and the appropriate treatment commenced. Microscopic examination of the urine revealed many red blood cells, hyaline and granular casts.

On August 4th, 1942, the patient suffered an accidental antepartum haemorrhage, subsequently came into labour and expelled a premature and stillborn infant. Throughout the day she was lethargic, drowsy and vomiting; and the blood urea was 74 mg. per 100 c.c. of blood. Only 60 c.c. of urine, containing "one-third deposit" of albumin, were secreted.

On August 5th, 1942, little more than 90 c.c. of urine were secreted, and it became solid with albumin on boiling. The blood urea was 98 mg. per 100 c.c. of blood, the oedema of the lower limbs was still marked, the vomiting was less.

On August 6th, 1942, the urinary output rose to 720 c.c., the blood-pressure had fallen to 150/95 mm. Hg. and the albuminous deposit to one-sixth, with a corresponding improvement in the general condition.

Subsequently, the daily urinary output varied from 75 c.c. to 1,050 c.c. per day, the blood urea was 65 mg. per 100 c.c. of blood on August 10th and, on August 13th, some red blood cells and a few casts were still present on microscopic examination of the urine.

A very relevant aspect of the management of acute diseases of the kidney complicating pregnancy is the place of therapeutic induction of abortion or of premature labour.

Although it is characteristic of these conditions that the haematuria, oedema and albuminuria persist in spite of delivery, it is nevertheless true that the tendency towards faulty water elimination, oedema, albuminuria and abnormal fat metabolism observed even in normal pregnancy is likely to aggravate the course of an acute nephritis or nephrosis.

Wegner⁷ reported that, in a series of 10,596 women whose pregnancies were reviewed, there were 10 cases of acute glomerulonephritis and 3 of acute nephrosis, an incidence of 0.056 and 0.025 per cent respectively. In every case the renal condition appeared to be aggravated as the pregnancy advanced and the mortality rate was 33.3 per cent for each condition.

RENAL FAILURE FOLLOWING TRANSFUSION REACTIONS DUE TO INCOMPATIBILITY INVOLVING THE RH FACTOR.

Unfavourable reactions following the transfusion of whole blood to recently confined patients, with evidence of intravascular haemolysis, icterus, and suppression of urine, have been noted with concern from time to time, especially as these reactions had usually occurred after transfusions given under the most favourable conditions, and after apparent compatibility had been established by the usual methods of blood typing and cross matching.

A cause of incompatibility reactions which may lead to a fatal anuria, and one of especial significance in obstetric practice, is the Rh property of human blood, and the recent (1940) work initiated by Landsteiner and Wiener⁴ in this connexion is now universally recognized. Especially important is the appreciation of the fact that, in obstetric practice, it is not necessary for a woman to be given a second transfusion before incompatibility reactions involving the Rh factor can occur. There seems little reason to doubt that the conception of isoimmunization in the human body by the Rh factor is a correct one, and the evidence on this score is now well known.^{5, 6}

When the original work on the Rh factor was published, it soon became apparent that it would have especial implications when applied to obstetric practice, and the study of renal failure in this field calls for

further consideration of the factors involved. Renal failure following the transfusion of incompatible blood is dependent on intravascular haemolysis and is unlikely to follow simple agglutination of the donor cells.⁷

Only about 30 per cent of immune sera will haemolyse as well as agglutinate red cells containing the corresponding agglutinin,⁸ but it is important to note that, even when agglutination occurs *in vitro*, intravascular haemolysis may occur *in vivo*. Thus, although haemolysis never occurs *in vitro* when Rh positive cells are incubated with sera containing Rh antibodies, there is abundant evidence (*et al.*) that severe intravascular haemolysis may follow the transfusion of Rh positive blood to a recipient possessing anti-Rh agglutinins in her serum.

The titre of the incompatible agglutinins in the recipient's plasma and the rate of transfusion appear to determine the mode of destruction of the donor's cells.⁸

Fairley,¹⁰ pointed out that haemoglobin liberated by intravascular haemolysis may be dealt with in three different ways:

(a) It may be absorbed by the reticulo-endothelial system and converted to bilirubin which is then discharged into the blood-stream and excreted by the liver. This is probably the only mechanism necessary when the haemolysis is slight.

(b) When the haemolysis is of greater degree, part of the haemoglobin is broken down intravascularly and haematin is liberated. This combines with serum albumin to form methaemalbumin which may, if in sufficient concentration, be recognized on spectroscopic examination.

(c) Some haemoglobin is excreted by the kidneys, but apparently⁷ a concentration of 135 to 180 mg. of haemoglobin per 100 c.c. of plasma (approximately equivalent to the rapid haemolysis of 60 c.c. of blood) is necessary for this to occur, although once

commenced haemoglobinuria may continue at lower plasma haemoglobin levels.

If the urine is alkaline most of the haemoglobin will be present in the form of oxyhaemoglobin and the urine will be red.

If the urine is acid or neutral methaemoglobin will be formed; acid haematin will be deposited in the renal tubules and casts of this substance may be found in the urine, which is dark in colour.

Following intravascular haemolysis, some degree of renal failure may occur with oliguria and a progressive increase in the blood urea estimations.

Baker and Dodds¹¹ expressed the opinion that the renal insufficiency in these cases was due to blockage of the renal tubules with acid haematin, a relatively insoluble compound which is formed in urine of high acidity and salt concentration. They were able to prevent the onset of renal failure in rabbits, to whom haemoglobin solutions had been given intravenously, by alkalizing the urine. Baker¹² further elaborated this point in 1939.

This conception, however, has been opposed by others, including De Navasquez,¹³ who believes that the anuria is the result of a diminished blood flow through the renal glomeruli, and by DeGowin *et al*¹⁴ who expressed the opinion that, in man, blockage of the renal tubules is insufficient in many cases to account for the degree of renal failure and postulated tubular damage by some "nephrotoxic factor" as the cause of the anuria.

Clinically, signs of uraemia may not be apparent until the 3rd or 4th day after the transfusion of incompatible blood. Thereafter a critical phase develops between the 6th and the 12th days, during which time the patient may become comatose and die, or may start passing large quantities of urine and recover.

A reduction in the incidence of severe or

fatal anuria following intragroup transfusion reactions in pregnant or puerperal women may be expected as a result of the wide interest which has been aroused in the clinical application of knowledge relating to the Rh factor. It is now unlikely that the husband of a woman who had given birth to an infant suffering from erythroblastosis foetalis would inadvertently be allowed to act as a blood donor to his wife even though his blood were compatible by the usual standards.

Nevertheless, the possibility exists of antibody production in the mother's serum of insufficient titre to cause erythroblastosis foetalis but sufficient to cause a troublesome reaction if the patient should be transfused with the husband's blood.⁶ Until such time as all laboratories concerned with pre-transfusion tests for obstetric cases are equipped to carry out the special cross-matching technique¹⁵ for demonstrating Rh incompatibility, the husband should not be regarded as a suitable donor for pregnant or puerperal patients.

The following case record illustrates very clearly the type of haemolytic transfusion reaction, almost certainly involving the Rh factor, encountered prior to the publication of Landsteiner's work on this subject:

CASE 4.

Mrs. M. R., aged 29 years, had had 3 normal infants, but her 4th pregnancy had terminated in the birth of a stillborn hydropoid infant in March 1937.

On September 25th, 1939, she was delivered of a stillborn macerated foetus which manifested the ascites and generalized oedema so characteristic of this form of erythroblastosis foetalis. The placenta, too, was hyperplastic and oedematous.

A pronounced hypochromic anaemia had been present during the latter weeks of the pregnancy; on September 21st the erythrocytes numbered 2,530,000 per c.mm. and the haemoglobin value was estimated as 30 per cent. Although there was no postpartum haemorrhage at the time of confinement, it was felt that the patient's convales-

cence would be hastened and her general condition improved by a blood transfusion during the puerperium.

On September 28th, therefore, the blood groups of the patient and her husband were investigated and both were found to belong to Group O. Direct cross-matching tests were satisfactory. On September 30th 600 c.c. of citrated blood were given into the patient's cubital vein; the donor being the husband.

A rise of temperature to 102°F. followed within a few hours of the transfusion and the patient complained of some tightness in the chest. The next day, October 1st, she was deeply jaundiced and catheterization produced only 15 c.c. of concentrated acid urine.

Following Baker's suggestion that renal failure in these circumstances might be averted by *effectively and rapidly alkalizing the urine*, efforts were directed towards this end. An alkaline compound prepared commercially for intravenous use was administered by this route, and an alkaline mixture was given by mouth every 2 hours.

In an endeavour to ascertain the cause of the reaction the blood of both the recipient and the donor was retyped and cross matched, but no agglutination could be detected after the patient's serum and the donor's red cells had stood in the incubator for 50 minutes. (This can now be explained¹⁶ by the fact that the transfused cells would have temporarily absorbed most of the recipient's serum agglutinins.)

On October 2nd, the patient's condition was much the same; the jaundice was still present and the urinary output was only 21 c.c. for the 24 hours. During the afternoon, 500 c.c. of a 25 per cent glucose solution were given intravenously as an empirical procedure.

On October 3rd the jaundice was less intense and the urinary output was 112 c.c., the urine being now alkaline in reaction. A blood count revealed 2,300,000 red cells per cubic millimetre and a haemoglobin value of 27 per cent.

On October 4th 196 c.c. of urine were secreted and, on subsequent days, the 24 hours' urinary output was as follows: October 5th, 168 c.c.; October 6th, 660 c.c.; October 7th, 1,800 c.c.; October 8th, 1,290 c.c.; October 9th, 1,560 c.c.; October 10th, 2,250 c.c.; October 11th, 3,110 c.c.

The jaundice had disappeared by the end of the

1st week after the transfusion, and the blood count gradually improved with iron therapy.

OBSTETRIC SHOCK—MATERNAL BIRTH TRAUMA AND CONCEALED RETROPLACENTAL HAEMORRHAGE.

Whatever views may be held on the aetiology of obstetric shock, the factors responsible for the oliguria do not differ materially from those encountered in non-obstetric or surgical shock.

In these cases, the renal failure is usually transient (assuming recovery from the shocked condition) and may rightly be attributed to the profound circulatory disturbance. The oligæmia and vascular hypotonia lead to a reduced blood volume passing through the glomeruli, and to a diminished filtration pressure respectively.

The oliguria usually responds to those measures normally put into operation (including the intravenous administration of blood serum) to combat the shock. If the patient does not respond to these measures and death occurs, it will not be because of the renal failure which is primarily symptomatic.

A form of renal failure is, however, occasionally encountered in obstetric practice in which the element of maternal birth trauma appears to play an important aetiological rôle. In other cases, the renal sequelae have followed a concealed (retroplacental) accidental haemorrhage.

As Young¹⁷ has pointed out, there is the same clinical sequence irrespective of whether the tissue damage occurred as the result of a prolonged and difficult labour or developed as a consequence of a retroplacental haemorrhage.

1. There is the initial tissue damage.
2. In severe cases, there is shock which may or may not be fatal. In those patients who survive, there develops:
3. Evidence of renal failure with oliguria

and a rising blood urea which usually reaches its peak between the 5th and the 9th days, and which is followed either by death or by an increasing diuresis and eventual recovery.

A further point of interest lies in the close resemblance between these two clinical states and the "compression syndrome." Instances have been reported¹⁸ in which patients, though successfully passing through a period of shock after a prolonged and difficult labour, subsequently developed renal failure and died; and most obstetricians will recall similar happenings in their experience.

In the reported cases, however, the histological lesions in the kidney closely resembled those described by Bywaters and Beall in 1941,¹⁹ and more fully by Bywaters and Dible in 1942.²⁰

These consist of degenerative and necrotic lesions of the tubular epithelium and the presence of pigmented casts in the lumina. A raised serum potassium level and myohaemoglobinuria were also present. The matrix of the casts was considered, on histological grounds, to be composed, not of red corpuscles, but of desquamated epithelial cells, and the pigmentation was attributed to the excretion from the blood-stream of myohaemoglobin.

Whether a "compression syndrome" comparable with that described by Bywaters and Beall exists in obstetric practice, as has been suggested, awaits the accumulation of further clinical biochemical and pathological data.

Although clinical details only are available, reference may be made to the following case report:

CASE 5.

Mrs. R. S., aged 21 years, a previously healthy primipara, was admitted to hospital on July 27th, 1940, as a case of failed forceps. Labour had been in progress for 2 days and, although dehydrated and exhausted, the patient was not appreciably

shocked. Catheterization on admission produced only 60 c.c. of concentrated blood-stained urine.

Delivery was effected by a lower segment Caesarean section. Post-operative treatment followed the usual lines and 2,000 c.c. of normal saline were given by an intravenous drip during the next 12 hours to combat the dehydration to which the initial oliguria was attributed.

On July 28th the patient's condition was generally satisfactory during the morning but she became confused and restless towards evening. Although fluids were being taken readily by mouth, only 115 c.c. of urine were secreted during the day.

On July 29th the blood urea was 113 mg. per 100 c.c. of blood and the oliguria persisted. A small blood transfusion (350 c.c.) was given during the day from a compatible female and unrelated donor.

On July 30th the patient was comatose, urine was not secreted and uraemic vomiting and twitching developed. Death occurred during the day but consent for autopsy could not be obtained.

The one feature common to all air-raid casualties exhibiting renal failure, not obviously due to other causes, was the evidence of compression of muscle tissue for varying periods, but usually from 6 to 9 hours. Some degree of muscle necrosis was also present but often to a limited degree.

It has been shown by Baetjer²¹ that when muscle fibres are injured their permeability increases and intracellular ions, such as potassium, are rapidly lost. (Increase in serum potassium levels was a constant finding in these cases.)

The injured muscle fibres also liberate a pigment known as myohaemoglobin which differs from haemoglobin in several ways. It has a smaller molecule, and the renal threshold for this substance is much lower than for haemoglobin, explaining the reason why none of the pigment is seen in the blood-stream in these cases.

Bywaters, Delory, Rimington and Smiles²² identified the pigment in the urine of cases exhibiting the compression syndrome as being identical with myohaemoglobin extracted from traumatized and

perfused human muscle. The significance of this lay, not so much in the fact that myohaemoglobin might be the cause of the renal failure, but in that it definitely incriminated muscle damage in this connexion.

It would appear, in the light of present knowledge, that the association between compression of muscle tissue and subsequent renal failure is based on the following possibilities:

(1) That the urinary failure follows tubular obstruction due to the formation of pigmented casts, the pigment being myohaemoglobin liberated from compressed muscle fibres, rapidly excreted owing to the small size of its molecule and precipitated in the renal tubules in the presence of a concentrated, acid urine. Evidence of the correctness of this conception would lie in the prevention of renal failure in these circumstances by maintaining an alkaline urine.

(2) That, at least, a contributory factor to the renal failure may be found in the high serum potassium level which may well exert toxic damaging effects on renal tubular epithelium.

In how far do these pathological and biochemical data apply in cases of renal failure following maternal birth trauma, and what is the rôle of retroplacental haemorrhage in producing renal sequelae?

The possibility of damage to the muscular structures of the pelvic floor being a source of myohaemoglobin is unconvincing, for the characteristic lesion in this area is a laceration and overstretching rather than a compression of muscle fibres. However, should the foetal head remain impacted for any length of time at the brim of the pelvis, compression of the soft muscular tissues of the birth canal between the foetal skull and bony pelvis could certainly occur.

On the other hand, the amount of muscle tissue subjected to compression would be small and, except in tonic contraction of

the uterus, the compressing force would be intermittent rather than continuous. However, this fact might favour the production of renal sequelae by allowing early access to the blood-stream of potassium and myohaemoglobin.

Estimation of serum potassium levels, examination of the urine for myohaemoglobin and, if death occurs, careful histological examination of the kidneys should be carried out in those obstetric cases which exhibit signs of progressive renal failure after a prolonged and difficult labour. Therapy might well be directed towards alkalinizing the urine.

The evidence relating to the other obstetrical condition which may be followed by renal failure, namely concealed (retroplacental) haemorrhage, is complicated by the pre-eclamptic or eclamptic phenomena which so frequently accompany it, and it is significant that blood pigment casts and tubular degeneration with haemoglobinuria have been described in fatal cases of eclampsia.

Nevertheless, there is reason to believe that the concomitant toxæmia is not necessarily the cause of the renal failure in the accidental haemorrhage syndrome.

Bywaters and Belsey in a later publication²³ quote cases in which renal failure developed following severe ischaemia of muscle not due to direct compression but resulting from prolonged arterial spasm or rupture of a main artery, a state of affairs, surely, comparable with the massive ischaemic lesion found in severe cases of retroplacental haemorrhage with involvement of the myometrium.

Bratton²⁴ found renal lesions resembling those of the crush syndrome in 6 fatal cases of antepartum haemorrhage with anuria or oliguria, none of the patients had been given a blood transfusion. Young¹⁷ gave details of 3 more fatal cases all with a history of accidental haemorrhage followed in 2 cases

by progressive renal failure and death in uraemic coma on the 9th and 10th days. (One patient died on the 1st day, presumably from shock and blood loss.)

A report from Professor Dible on the histological appearance of the kidney is quoted. Referring to Case 2, he states: "The picture is practically indistinguishable from that found in the kidney in cases of the crush syndrome," and, of Case 3, he reports: "The picture is essentially similar to that found in the kidney in the fatal anuria of the crush syndrome."

Referring again¹⁷ to the matter of an aetiological relation between the retroplacental haemorrhage and the subsequent renal failure, evidence can readily be adduced to show that renal failure does not follow other types of obstetrical haemorrhage, viz. postpartum haemorrhage and haemorrhage due to placenta praevia.

Admittedly, shock is more marked in concealed accidental haemorrhage, but the time of onset of renal failure in those cases studied precluded the possibility of shock being responsible for the renal sequelae.

The frequent association of pre-eclampsia and eclampsia with accidental haemorrhage certainly tends to incriminate the toxæmia as a possible cause of the anuria. But renal failure is by no means a constant feature in eclampsia, and in at least one of the reported cases a fatal anuria followed an accidental haemorrhage to which trauma rather than toxæmia appeared to have contributed. On the other hand, it must be admitted that, in spite of the close analogy between uteroplacental apoplexia and other types of massive muscle ischaemia, the former lesion may be present in a marked degree without subsequent renal failure.

Thus the available evidence is obviously incomplete but the subject merits further investigation. That premature conclusions should not be drawn as to cause and effect in the accidental haemorrhage—renal

failure syndrome is perhaps shown by the following case report. It tells of a woman who died from renal failure on the 9th day following a concealed accidental haemorrhage, but in whom the renal failure could not be accepted (for reasons shown at autopsy) as the result of the haemorrhage.

CASE 6.

Mrs. H. J. was a primipara, aged 28 years, who was delivered, at term, of a stillborn macerated foetus at 3.15 a.m. on March 6th, 1944, following an accidental (retroplacental) haemorrhage. She had been receiving treatment privately, over a short period, for raised blood-pressure. There was no appreciable degree of shock at the time of confinement but 21 hours later (i.e. up till midnight on March 6th) only 165 c.c. of urine had been secreted.

On March 7th, the 24 hours' urinary output was only 60 c.c. and, on March 8th, it was 75 c.c. The blood-pressure was 150/95 mm. Hg. and a deposit of albumin was present in the urine. The patient was drowsy and there was frequent vomiting of brownish fluid.

On March 9th, however, 300 c.c. of urine were secreted, followed by 750 c.c. on March 10th; vomiting had ceased but the patient was oedematous and semi-comatose. Subsequently, there was little change in the clinical picture; the urinary output was 690 c.c. on March 11th, 630 c.c. on March 12th, 1,815 c.c. on March 13th, and 2,040 c.c. on March 14th; but, in spite of the relative diuresis death occurred at 9.0 a.m. on March 15th.

At autopsy, the kidneys were found to be pale and oedematous; histologically there was some diffuse cast formation but these did not resemble myohaemoglobin casts. The general histological appearance of the kidney was that of an "arteriosclerotic nephrosclerosis with shrinkage and hyaline obliteration of many glomerular tufts, focal interstitial fibrosis, and capillary dilatation of remaining tufts."

SYMMETRICAL CORTICAL NECROSIS OF THE KIDNEYS.

Renal failure is the prominent and characteristic feature of this condition which is not peculiar to pregnancy but, nevertheless,

is most frequently associated therewith, especially when the pregnancy has been complicated by a pre-eclamptic or eclamptic toxæmia.

A coincident accidental hæmorrhage has been noted in a significant proportion of cases. Although alternative theories have been put forward, there is reason to believe that the condition is due to spasm of the terminal arterioles of the kidney with resultant thrombosis and ischaemic necrosis leading to the production of a typical zone of necrotic cortex varying in depth, but forming a complete covering around the kidney. Evidence of stasis is present in the arterioles supplying the renal cortex.

Clinically, the condition is characterized by an extreme oliguria passing on to an anuria, a transient hæmaturia in the early stages, and a gradually progressive uræmia which often kills the patient in from 6 to 14 days, the clinical picture thus resembling, in many ways, that of a surgical anuria.

In spite of the rarity of the disease and the impossibility of establishing a definite diagnosis without biopsy or autopsy, the development of the clinical syndrome described in a patient suffering from a severe pregnancy toxæmia, especially if complicated by an accidental hæmorrhage, would justify a provisional diagnosis of symmetrical cortical necrosis of the kidneys.

The question naturally arises as to whether any special aetiological significance may be attached to the frequently associated accidental hæmorrhage in view of the evidence that the latter condition may, *per se*, be a cause of subsequent renal failure. The kidney pathology, both gross and histological however, presents such striking differences in the two conditions that a common aetiology would seem unlikely.

The accidental hæmorrhage rate is likely to be high in any series of severe toxæmias (such as usually precede cortical necrosis of the kidneys), and it is probable that the

more common retroplacental hæmorrhage and the occasional case of symmetrical cortical necrosis are both manifestations of the toxic damage to vascular endothelium and the general vasomotor irritability so characteristic of the pregnancy toxæmias.

A point of practical importance is whether there is a stage in the sequence of events leading up to the condition of cortical renal necrosis, as seen in the autopsy room, when the restoration of normal vasomotor tone might lead to the recovery of renal function before the formation of secondary thrombi had produced the ischaemic necrosis.

The experimental work of Ricker²⁵ that terminal vascular segments of a tissue respond to weak irritation by vasodilatation and hyperæmia, to medium irritation by vasoconstriction and ischaemia, and to strong irritation by proximal vasoconstriction and peripheral vasoparalysis (with resultant thrombosis), suggests that the formation of actual thrombi may represent a comparatively late stage in a process initiated by the pregnancy toxæmia which, I feel, may be regarded, in these cases, as the source of the irritant just as chemical irritants (ethylene glycoll) have been incriminated in other reported instances of cortical necrosis unassociated with pregnancy.²

Actually, of course, the majority of cases do occur as a complication of pregnancy toxæmias, and the reason may lie in the consequent presence of additional factors predisposing to intrarenal thrombosis, viz. a general (and intrarenal) vasomotor instability producing a ready response to circulating irritants, toxic damage to vascular endothelium and, possibly, an increased coagulability of the blood, all tending to favour the formation of thrombi.

It seems worth attempting to correlate Ricker's conception of the 3 stages in the pathogenesis of cortical necrosis with the clinical course of the disease, thus:

Stage 1. Renal (cortical) hyperaemia due to vasodilatation with increased blood supply within the kidney but a reduced blood-flow through the glomeruli. The latter condition would explain the initial oliguria, and the former the transient haematuria.

Stage 2. Renal (cortical) ischaemia due to vasoconstriction. Clinically, this would be manifested by a more severe degree of urinary suppression, often amounting to an anuria, the disappearance of blood from the urine and a rise in the blood-nitrogen level.

Stage 3. Renal (cortical) necrosis of ischaemic origin following the formation of thrombi as described. This would be characterized, clinically, by an almost complete anuria leading to azotaemia, terminal uraemic manifestations (these may be absent in some cases) and death towards the end of the 2nd week.

If such correlation between the clinical and pathological data be accepted, it is clear that the possibilities of recovery may exist during the 1st and 2nd stages of the development of complete cortical necrosis. The irreversible changes characteristic of the 3rd stage could, perhaps, be prevented if, during the 2nd stage:

(a) the arteriolar vasoconstriction could be relieved, if only temporarily, in the first instance; and

(b) some diuretic substance could increase the excretory capacity of such cortical tissue as may thus have been relieved of its ischaemic condition.

The case report to be quoted suggests, even admitting the possibility of spontaneous recovery, that the repeated intravenous administration of hypertonic glucose solutions may act in such a way.

Dieckmann,² discussing the treatment of the oliguria of eclampsia by this method, expresses the opinion that the rapidity of the diuresis effected by parenteral hyper-

tonic glucose, indicates that the urinary suppression is due to arteriolar spasm rather than to oedema of the kidney. Examination of the capillaries of the nail bed during such treatment revealed definite improvement in the circulation, including the disappearance of beading in some cases.

That such relief of vasoconstriction may, initially, be only transient unless the treatment were repeated, would not necessarily detract from its value in cortical necrosis for the diuresis, which in a favourable case would follow, may so effectively rid the blood-stream of irritant toxins that the stimulus to a return of the vasospastic state would be lacking. (To what extent is the fall in blood-pressure of the post-eclamptic patient the result of the diuresis which so often accompanies recovery?) Moreover, there are no great technical difficulties in repeating the treatment if careful selection of veins is exercised. The clinical details of the case referred to are as follows:

CASE 7.

Mrs. V. T. was a primipara, aged 22 years, who, prior to her confinement on September 6th, 1942, had been treated for pre-eclamptic toxæmia. There had not been any accidental haemorrhage. Just before the delivery 75 c.c. of urine had been withdrawn from the bladder by catheterization but there was no further urinary secretion during the day (the confinement having taken place at 7.0 a.m.). The patient was admitted to hospital at this stage.

On September 7th there was complete anuria but the patient looked well and stated that she felt well. There was no oedema.

On September 8th 45 c.c. of blood-stained urine were obtained by catheterization, making a total of 120 c.c. of urine secreted in 3 days.

The blood urea was estimated to be 196 mg. per 100 c.c. of blood. Only a cloud of albumin was present in the urine. The patient was inclined to be drowsy but otherwise seemed well; 500 c.c. of 25 per cent glucose solution were given intravenously.

On September 9th 390 c.c. of urine were secreted. Albumin or blood were not present and microscopic examination failed to reveal any casts.

The blood urea was 208 mg. per 100 c.c. of blood and the general condition of the patient was unchanged. The blood-pressure readings, which had previously shown considerable fluctuation, were now consistently within normal limits (120 mm. Hg.). A further 1,200 c.c. of 25 per cent glucose solution were given intravenously.

On September 10th 900 c.c. of urine were secreted and, during the next 4 days, the 24 hours' output measured 1,560 c.c., 2,040 c.c., 1,890 c.c., and 2,520 c.c. respectively, and continued at a satisfactory figure thereafter.

Nevertheless, the blood urea was till 260 mg. per 100 c.c. of blood on the 7th day after admission, 147 mg. per 100 c.c. on the 12th day, and 65 mg. per 100 c.c. on the 21st day.

Clinically, the improvement in the condition of the patient herself began on the 4th day after admission and continued steadily thereafter, preceding at all stages the fall in the blood urea estimations.

SUMMARY.

1. The subject of renal failure from the point of view of the obstetrician is introduced by a recapitulation of some relevant facts of renal physiology.

2. The pharmacology of various diuretic substances is discussed.

3. The pathogenesis, clinical features, lines of investigation and methods of treatment of renal failure as encountered in obstetric practice are considered with especial reference to eclampsia, acute glomerulonephritis, renal failure occurring as a sequel to transfusion accidents involving the Rh factor, as a sequel to concealed accidental haemorrhage or following a prolonged and difficult labour.

4. Symmetrical cortical necrosis of the kidneys is also considered in some detail, and certain suggestions are made linking pathogenesis, clinical manifestations and treatment.

5. Typical case records are quoted illustrating each of these different clinicopathological types of renal failure.

CONCLUSIONS.

It is obvious that there are still many gaps in our knowledge of the factors involved in the development of renal failure complicating obstetrical conditions.

Therapy, however, is becoming more rational as evidence accumulates of the underlying pathology and biochemistry of the various clinical types of renal failure.

Further development may be expected in this field of investigation.

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The Definition of Prematurity

A Proposed Minimal Weight Standard for Viable Premature Infants.

BY

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It is unfortunate that a minimal weight standard for viable premature infants was not adopted concurrently with the maximal weight standard of $5\frac{1}{2}$ pounds ($2\frac{1}{2}$ kilograms). The weight range of viable premature infants would thus have been exactly defined and a scientific basis provided for statistics relating to them. McNeil,¹ in a Finlayson Memorial Lecture, drew attention to the desirability of adopting a minimal weight standard of viability, and pointed out that the absence of a universal minimal standard makes the comparison of figures relating to the frequency and mortality of premature infants almost valueless. The rectification of this omission is overdue and a minimal weight standard is proposed in this paper. The suggested standard has been formulated by comparing the estimated period of gestation with the birth-weight in a large number of premature infants, and finding the average weight of infants with an estimated gestation period of 28 weeks—the age at which the foetus is generally presumed to become viable.

A weight standard of viability of 1,000 g. (2 pounds, 3.2 ounces) has been adopted by some workers, particularly in the United States, while others regard infants of less than 1,500 g. (3 pounds, 4.8 ounces) as non-viable. Various weight standards between these two extremes are also in use.

The Maximal Weight Standard of $5\frac{1}{2}$ Pounds.

This upper-weight standard of prematurity, which was not officially adopted in the English-speaking countries until the later year of 1930, has been advocated and used by various authorities for many years. Ylppö,² in his classical treatise on prematurity, defined as premature those infants with a birth-weight under 2,500 g.: he advocated, on both clinical and statistical grounds, the universal adoption of this standard as the most desirable arbitrary dividing-line between mature and premature infants. Ylppö's work had great influence on the European Continent, where the standard of 2,500 g. or less soon became general. This standard was also used by numerous workers in the United States prior to its official adoption by the American Academy of Pediatrics in 1935. The Academy defined prematurity in the following terms: "For statistical purposes and comparison of results of care, a uniform standard for diagnosis of prematurity is important. A premature infant is one who weighs 2,500 g. or less at birth (not on admission) regardless of the period of gestation. All liveborn premature infants should be included, evidence of life being heart-beating or breathing."³

In Great Britain an incomplete period of gestation continued to be the criterion of prematurity until 1938, when a joint

committee of the Royal College of Physicians of London and the Royal College of Obstetricians and Gynaecologists was appointed to recommend a more suitable definition of prematurity. The committee adopted the following standard: "That in conformity with the standard in international use an infant whose birth-weight is $5\frac{1}{2}$ pounds (approximately 2,500 g.) or less should be considered, for the purpose of comparison of records, as either immature or prematurely born, according as the estimated period of gestation is full-time or less." The reservations in the latter part of this definition bear the imprint of compromise and seem unnecessarily to impair its clarity; they have been ignored in practice and the more precise American standard, which states that "a premature infant is one who weighs 2,500 g. or less at birth regardless of the period of gestation," has been generally adopted in this country.

premature weigh 6 to 7 pounds or more; (c) The frequency with which infants judged to be mature weigh $5\frac{1}{2}$ pounds or less. The weight of $5\frac{1}{2}$ pounds (2,500 g.) is the most suitable arbitrary dividing-line between mature and premature infants for two main reasons: (a) Because infants below this weight require special nursing care and special feeding methods. (b) Because $5\frac{1}{2}$ pounds corresponds exactly with $2\frac{1}{2}$ kg., an essential correspondence between the avoirdupois and metric systems which cannot be obtained in round figures at any other point in the neighbourhood of 5 to 6 pounds.

Relation of Birth-Weight and Estimated Period of Gestation in 1,041 Liveborn Premature Infants (Twins Excluded).

This is shown in tabular form (Table I) and graphically (Fig. 1). Twin infants totalling 252 have been excluded because

TABLE I.

Relation of Birth-weight and Estimated Period of Gestation in 1,041 Liveborn Premature Infants (Twins Excluded).

| | Weight in pounds | | | | | | | |
|---|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|---------------------|
| | $5\frac{1}{2}$ to 5 | 5 to $4\frac{1}{2}$ | $4\frac{1}{2}$ to 4 | 4 to $3\frac{1}{2}$ | $3\frac{1}{2}$ to 3 | 3 to $2\frac{1}{2}$ | $2\frac{1}{2}$ to 2 | 2 to $1\frac{1}{2}$ |
| No. of infants | 423 | 207 | 146 | 90 | 75 | 44 | 34 | 22 |
| Period of gestation (average in weeks) | 37.6 | 35.9 | 35.0 | 33.0 | 31.6 | 28.9 | 27.7 | 26.4 |

The introduction of this maximal weight standard of prematurity has proved to be of great value for statistical purposes. Both obstetricians and paediatricians have found it much more satisfactory than an estimated incomplete period of gestation, which had always been the criterion of prematurity up to that time. The principal drawbacks of the old definition are (a) The frequent uncertainty regarding the date of onset of the last menstrual period; (b) The frequency with which infants judged to be

the average period of gestation is greater in twin infants than in single infants of a corresponding weight. This fact necessitates their exclusion in determining the normal relation between the birth-weight and the period of gestation, because the proportion of twin infants differs in each weight group. Stillborn and deadborn premature infants have also been excluded from this calculation because, in their case, the relation of the weight and the foetal age is very variable owing to the frequency of

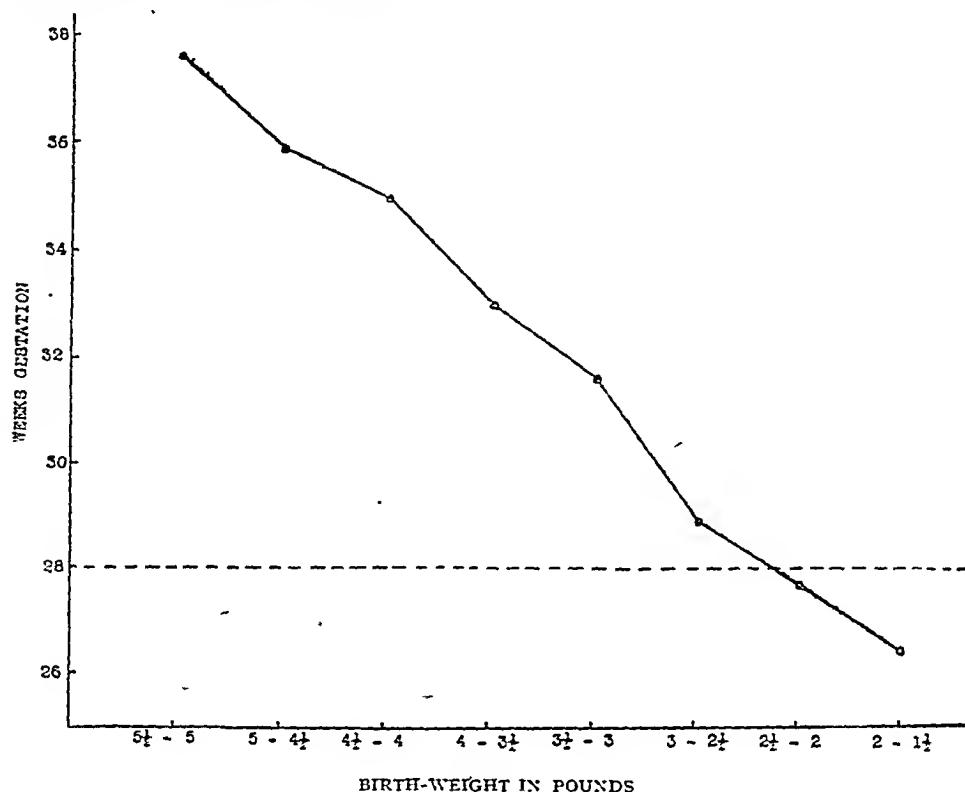


FIG. 1.

Relation of birth-weight and estimated period of gestation in 1,041 liveborn premature infants (twins excluded).

gross congenital defects and intra-uterine death. It will be observed that the 44 infants in the 3 to 2½ pounds weight group averaged 28.9 weeks gestation and the 34 infants in the 2½ to 2 pounds group averaged 27.7 weeks gestation. The lower-weight limit of viability would appear, therefore, to lie between 3 pounds and 2 pounds. There is an important reason why the average weight of infants of 28 weeks gestation cannot be accurately calculated from hospital records. It is dependent on the general practice of regarding many infants who have a gestation period of 26 to 28 weeks as viable, and recording them as being over 28 weeks gestation so that the mother will receive her maternity benefit. Such a practice would seem quite justifiable, for the duration of gestation is only

an approximate estimation and it is certainly right that the mother should receive the benefit of any doubt in borderline cases. From the statistical point of view, however, this practice vitiates the figures relating to the lower weight groups of premature infants, as a considerable number of pre-viable infants are notified as viable. The conclusion must be drawn, therefore, that the figure of 28.9 weeks exceeds the actual period of gestation in the 3 to 2½ pounds group and that the average weight of infants of 28 weeks gestation probably lies somewhere between 3 and 2½ pounds.

The Proposed Minimal Weight Standard.

The weight of 2¾ pounds (2 pounds, 12 ounces), which corresponds exactly with 1¼ kg. (1,250 g.), would appear, in view

of the evidence presented in this paper, to be the most desirable minimal arbitrary weight standard for premature infants.

The reasons for selecting this figure are as follows:

(1) The average weight of infants of 28 weeks gestation appears to lie between 3 and $2\frac{1}{2}$ pounds.

(2) The weight of $2\frac{3}{4}$ pounds avoirdupois corresponds exactly with the weight of $1\frac{1}{4}$ kg. (1,250 g.) in the metric system—a correspondence in relatively round figures which cannot be obtained at any other point in the neighbourhood of 3 to $2\frac{1}{2}$ pounds.

(3) The minimal figures of $2\frac{3}{4}$ pounds and $1\frac{1}{4}$ kg. are exactly half the maximal figures of $5\frac{1}{2}$ pounds and $2\frac{1}{2}$ kg. respectively, a fact which makes them easy to remember as the maximal figures are now in general use.

years period 1938 to 1943—an incidence of 7.9 pre-viable liveborn infants per 1,000 live-births. The total number of mature, premature and pre-viable liveborn infants in the 6-years period is given in Table II, also the incidence in each group.

Survival of Pre-viable Infants. Only 4 of the 118 pre-viable infants survived—a death-rate of 966 per 1,000. Three of these survivors were twins, who have a better chance of survival than single infants of a corresponding weight. This is a very low survival-rate but various authorities^{5, 6, 7} have demonstrated that much better figures are attainable. Nevertheless, even in the most ideal circumstances, the death-rate in infants with a birth-weight of less than 2 pounds, 12 ounces will always be very high. A comparison of the death-rate in

TABLE II.

The Incidence of Mature, Premature and Pre-viable Livebirths in a Total of 14,923 Livebirths at the Simpson Memorial Maternity Pavilion, Royal Infirmary, Edinburgh, in the 6-Years Period, 1938 to 1943.

| | | Infant Category. | | |
|---------------------|-----|--------------------------------------|---|---|
| | | Mature Over $5\frac{1}{2}$ pounds | Premature $5\frac{1}{2}$ to $2\frac{3}{4}$ pounds inclusive | Pre-viable Under $2\frac{3}{4}$ pounds |
| Number of infants | ... | 13,519 | 1,286 | 118 |
| Incidence per 1,000 | ... | 905.9 | 86.2 | 7.9 |

Liveborn Pre-viable Infants (under $2\frac{3}{4}$ pounds weight). The adoption of the proposed arbitrary minimal weight standard of $2\frac{3}{4}$ pounds would necessitate the provision of a separate category for liveborn infants weighing under $2\frac{3}{4}$ pounds. The term pre-viable, which is sometimes used in the case of very small premature infants, would suitably describe this category.

A total of 118 pre-viable (under $2\frac{3}{4}$ pounds) liveborn infants were born in the Simpson Memorial Maternity Pavilion, Royal Infirmary, Edinburgh, in the six-

each $\frac{1}{2}$ pound weight group between 4 pounds and 2 pounds shows a steep rise in the 3 to $2\frac{1}{2}$ pounds group, the one which is bisected by the proposed minimal weight standard of $2\frac{3}{4}$ pounds (Table III, Fig. 2). Subdivision of this group into a viable half (3 to $2\frac{3}{4}$ pounds) and into a pre-viable half ($2\frac{3}{4}$ to $2\frac{1}{2}$ pounds) shows (Table IV) that the chances of survival are much poorer in the pre-viable half, a fact which emphasizes the appropriateness of the proposed $2\frac{3}{4}$ pounds minimal weight standard for viable premature infants.

TABLE III.

The Number of Infants and the Death-rate in each Half-pound Weight Group Between 4 pounds and 2 pounds.

| | Weight group | | | |
|-----------------------------|----------------|----------------|----------------|----------------|
| | 4 to 3½ pounds | 3½ to 3 pounds | 3 to 2½ pounds | 2½ to 2 pounds |
| Number of infants | 139 | 98 | 68 | 58 |
| Number of surviving infants | 75 | 36 | 8 | 1 |
| Death-rate per 1,000 | 460.4 | 632.7 | 882.4 | 982.8 |

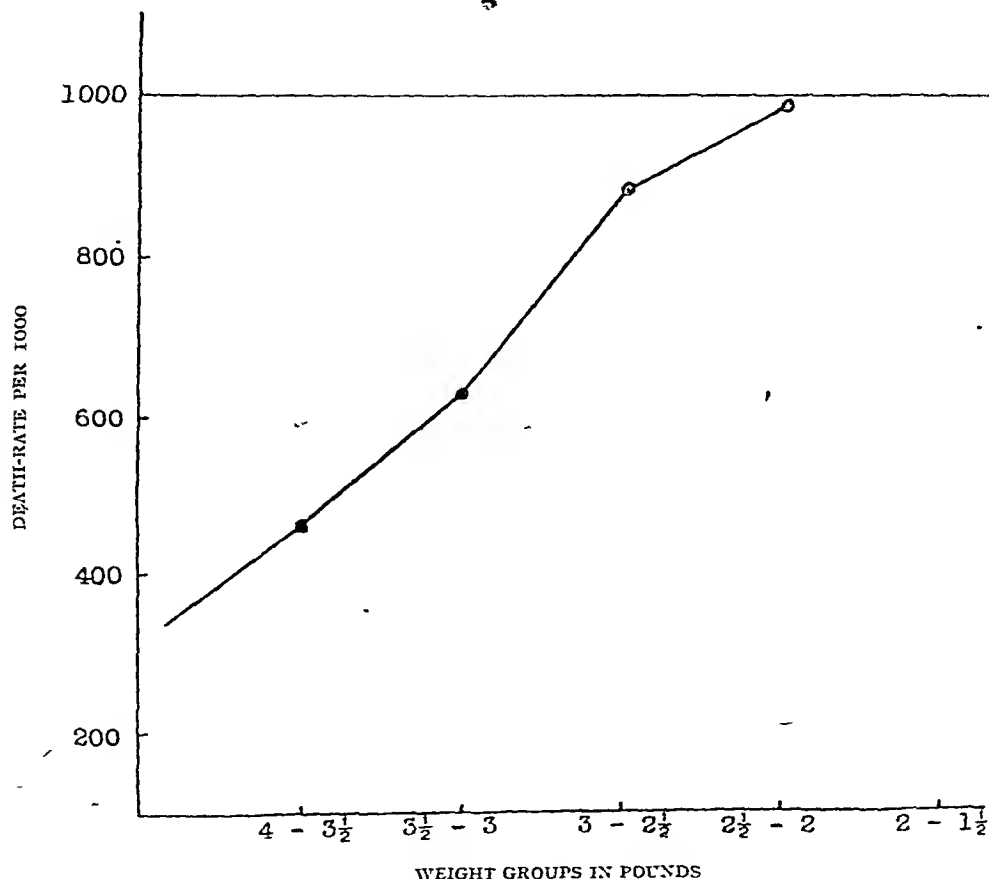


FIG. 2.

The death-rate in each half pound weight group between 4 pounds and 2 pounds.

Effect of the 2½ pounds Minimal Standard on the Classification of Stillbirths.

The substitution of the arbitrary weight standard of 2½ pounds for the time-honoured standard of an estimated gestation

period of 28 weeks would reduce considerably the proportion of premature stillborn foetuses falling into the category of viable stillborn infants, and increase correspondingly the proportion falling into the cate-

TABLE IV.

The Number of Infants and the Death-rate in the Viable half (3 to 2¾ pounds) and in the Pre-viable half (2¾ to 2½ pounds) of the 3 to 2½ pounds Weight Group.

| | Weight group | |
|------------------------------------|----------------------------|---------------------------------|
| | 3 to 2¾ pounds (Viable) | 2¾ to 2½ pounds (Pre-viable) |
| Number of infants | 40 | 28 |
| Number of surviving infants | 6 | 2 |
| Death-rate per 1,000 | 850.0 | 928.6 |

gory of pre-viable stillborn fetuses which are commonly termed miscarriages. The effect of this change of definition in the 6-years period at the Simpson Maternity Pavilion, referred to above, is shown in Table V. This table shows that 139 (27 per

in accordance with the universally acknowledged fact that the average weight of stillborn infants is considerably less than the average weight of liveborn infants at a corresponding period of gestation. The principal causes of the lower average

TABLE V.

The Effect of the 2¾ pounds Minimal Standard on the Classification of 1,108 Infants Classified as Stillbirths at the Simpson Maternity Pavilion, Royal Infirmary, Edinburgh, in the 6-years Period, 1938 to 1943.

| | Mature | Premature 5½ to 2¾ pounds inclusive | Pre-viable (Miscarriage) Under 2¾ pounds |
|---------------------|--------|---|--|
| Number of infants | 588 | 381 | 139 |
| Incidence per 1,000 | 530.6 | 343.9 | 125.5 |

cent) fetuses classified as premature stillbirths by the 5½ pound-28 weeks standard (the current definition of prematurity) would be classified as miscarriages by the 5½ pound-2¾ pound standard (the proposed new definition of prematurity). This figure of 27 per cent is much higher than the figure of 8.4 per cent which is the proportion of liveborn infants transferred to the pre-viable category by the substitution of the proposed new definition for the current definition. The great difference in the proportion of liveborn and stillborn infants who would be classified as pre-viable instead of viable, according to the proposed minimal weight standard of 2¾ pounds, is

weight of stillborn infants at a corresponding period of gestation are the common occurrence of gross congenital malformations such as anencephaly and of intra-uterine death occurring some weeks before birth.

The considerable reduction in the number of stillbirths which would follow the adoption of the 2¾ pounds standard would appear to be desirable, because a large proportion of the fetuses which would fall into the pre-viable (miscarriage) group would show either gross congenital malformations or maceration following intra-uterine death. Forty (29 per cent) of the 139 fetuses which would be classified as

miscarriages by the $2\frac{3}{4}$ pounds standard, instead of stillbirths by the current standard, showed gross congenital malformations; anencephaly accounted for 32. Accurate figures relating to intra-uterine death cannot be given but at least 20 per cent would probably fall into this category. Thirty-nine (28 per cent) of the 139 foetuses affected by the change of standard weighed less than 2 pounds at birth.

SUMMARY.

The desirability of adopting, for statistical purposes, an arbitrary minimal weight standard for viable premature infants has been discussed.

Minimal weight standards in use vary between 1,000 g. and 1,500 g.

The evolution of the international maximal standard of $5\frac{1}{2}$ pounds or less has been traced. It apparently originated on the European Continent.

The relation of the birth-weight and the estimated period of gestation in 1,041 live-born premature infants (twins excluded) has been investigated. The average weight of infants of 28 weeks gestation appears to be between 3 and $2\frac{1}{2}$ pounds.

A minimal arbitrary weight standard for premature infants of 2 pounds 12 ounces (1,250 g.) has been proposed for the following reasons: (a) The average weight of infants of 28 weeks gestation appears to be about $2\frac{3}{4}$ pounds. (b) The weight of $2\frac{3}{4}$ pounds avoirdupois corresponds to the weight of $1\frac{1}{4}$ kg. (1,250 g.) in the metric system. This correspondence in round figures is an essential condition of an international standard. (c) The minimal weight of $2\frac{3}{4}$ pounds is exactly half of the maximal weight of $5\frac{1}{2}$ pounds, a fact which simplifies the definition of the weight range of prematurity.

The term "pre-viable" has been proposed for the separate category of liveborn

premature infants with a birth-weight of less than $2\frac{3}{4}$ pounds.

A total of 118 pre-viable infants were born in a 6-years period at the Simpson Maternity Hospital—an incidence of 7.9 per 1,000 live-births. Only 4 survived—a death-rate of 966 per 1,000. Better figures are attainable, but the mortality of infants weighing less than $2\frac{3}{4}$ pounds at birth will always be very high.

The effect of the $2\frac{3}{4}$ pounds minimal standard on the classification of stillbirths has been discussed. In the 6-years period reviewed 27 per cent (139) of the premature foetuses classified as stillbirths ($5\frac{1}{2}$ pounds—28 weeks' gestation standard) weighed less than $2\frac{3}{4}$ pounds and would be classified as pre-viable (miscarriages) according to the proposed new definition.

A much larger proportion of stillborn infants of $5\frac{1}{2}$ pounds or less (27 per cent) than of liveborn infants of $5\frac{1}{2}$ pounds or less (8.4 per cent) would be excluded from the category of viable premature infants by the lower limit of $2\frac{3}{4}$ pounds than by the current lower limit of an estimated gestation period of 28 weeks. This would seem desirable as about half of the excluded stillborn foetuses in the period under review were cases of gross congenital malformation or of maceration following intra-uterine death.

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The Value of the Rhesus Test in Obstetrics

BY

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IN 1940, Landsteiner and Wiener¹ demonstrated the presence of the Rh factor in the red cells of 85 per cent of human beings. Following this, Wiener and Peters,² and Wiener^{3, 4} showed that certain individuals, whose red cells lacked this factor (Rh negative), were capable of producing an Rh antibody which would agglutinate the red cells of Rh positive persons. This production of Rh antibody could result from stimulation by either a previous transfusion with Rh positive blood or, in the case of women, by bearing an Rh positive child. Following this, Levine, Katzin and Burnham⁵ suggested that erythroblastosis foetalis, or as it is better called "haemolytic disease of the newborn," was due to the haemolysis of the infant's red cells by Rh antibody. According to their hypothesis, an Rh negative woman with an Rh positive husband and carrying an Rh positive foetus might become immunized by her infant's red cells and produce an Rh antibody which passed back through the placenta and caused haemolysis of the infant's red cells. This hypothesis has been amply confirmed by subsequent workers (Boorman, Dodd and Mollison,⁶ Race, Taylor, Cappell and McFarlane,⁷ Boorman, Dodd and Mollison,⁸ Kariher and Spindler,⁹ Potter, Davidsohn and Crunden¹⁰). Further recent work has shown that there are at least 7 Rh genes (Race, Taylor, Cappell and McFarlane¹¹) with 28 possible genotypes, and that in order to produce Rh antibody, a mother need not necessarily be

Rh negative (McCall, Race and Taylor¹²). Taylor and Race¹³ have also shown that the likelihood of a child suffering from erythroblastosis foetalis is considerably greater if the father is a homzygous Rh positive (genotype Rh Rh) than if he is heterozygous (genotype Rh rh).

Boorman and Dodd¹⁴ have shown that the Rh factor is present not only in the red cells but also in body fluids and in the cells of a number of tissues. This finding raises the possibility that Rh antibody might react with tissue cells and produce other effects than those of recognizable haemolytic disease. In this connexion it is interesting to note that Javert¹⁵ has found evidence of congenital abnormalities in 22 per cent of his cases of haemolytic disease of the newborn, though it should be noted that they were practically all instances of very minor abnormalities. Apart from this there is the possibility of other effects being produced in both mother and foetus by Rh antibodies, as for example repeated stillbirths, repeated abortions and possibly even toxæmias of pregnancy, since Javert¹⁵ has noted an association between eclampsia and hydrops foetalis.

During the past 18 months we have investigated the Rh reactions of 280 selected obstetrical cases. These were sent to us by our clinical colleagues either because they considered that the infants were suffering from haemolytic disease of the newborn or because they suspected that the Rh factor might be the cause of other obstetric mis-

haps of the types mentioned above. In brief, our results have confirmed those of other workers with regard to haemolytic disease of the newborn and we put forward evidence to support the existence of a 4th variant of this disease. We have failed to show a connexion between the Rh factor and any other condition and we publish these negative results in the hope of saving unnecessary investigations.

Technique. Whenever possible we have obtained sterile samples of whole, coagulated blood. From this, both cells and serum can be obtained and we have found that the red cells are better preserved this way especially when there is any delay, as in posted specimens. If possible we have left the whole specimen in the refrigerator at $2-4^{\circ}\text{C}$. over night and decanted the serum cold next morning in order to get rid of any possible cold agglutinins. The test has been done according to the technique of Boorman, Dodd and Mollison.⁶ At the beginning, before the various Rh genotypes were recognized, we relied on using several Rh antisera to detect Rh positive red blood cells. Later we were able to use sera containing known Rh antibodies (ρ , ρ_1 , and ρ_2). This is necessary because Rh positive red blood cells of certain genotypes do not agglutinate with the common Rh antibody (ρ), and, if this antibody alone is used, will be wrongly diagnosed as Rh negative. The serum was tested for antibody in all cases irrespective of the Rh group of the cells because it has been shown that Rh antibody may occur in an Rh positive individual (McCall, Race and Taylor¹²) and we have in fact encountered 5 such cases, 3 of them in this series. In testing for the presence of Rh antibody in the patient's serum it is necessary to use a series of Rh positive red blood cells of known genotype, otherwise certain of the rarer Rh antibodies (ρ_1 , or ρ_2) may be missed. It is also necessary to test the un-

known serum against known Rh negative cells firstly as a control and secondly because both Levine, Javert and Katzin¹⁶ and McCall, Race and Taylor¹² have discovered sera which agglutinate such cells.

Results. Our findings in this series of 280 cases are summarized in Table I.

TABLE I.
Distribution of Rh Groups Among 280 Cases.

| | No. | With Rh antibody | Without Rh antibody |
|--------|-----|------------------|---------------------|
| Rh + | 196 | 3 | 193 |
| Rh - | 84 | 58 | 26 |
| Totals | 280 | 61 | 219 |

Of the whole series 196 were Rh positive and 84 Rh negative. Rh antibody was demonstrated in 61 cases (Table II). Of these 53 were clinically recognizable examples of haemolytic disease of the newborn; the remaining 8 cases were atypical and will be discussed in detail later.

TABLE II.
Distribution of Cases with Demonstrable Rh Antibody.

| Form of haemolytic disease of the new born | Rh- | Rh+ | Total |
|--|-----|-----|-------|
| Hydrops foetalis | 8 | 0 | 8 |
| Icterus gravis ... | 27 | 0 | 27 |
| Haemolytic anaemia | 16 | 2 | 18 |
| Other cases .. | 7 | 1 | 8 |

In this series we have not encountered any examples of Rh antibody associated with a healthy baby, nor of clinical haemolytic disease of the newborn in the absence of Rh antibody though both have been observed by other workers (Boorman, Dodd and Mollison⁶), the haemolysis in the latter cases being apparently due to high titre anti A. or anti B. agglutinin.

It will be noted that in this series we encountered 3 Rh positive mothers whose sera contained Rh antibody. All 3 be-

longed to the rarer Rh positive genotypes (Rh₁Rh₁, Rh''rh, and Rh'rh) and their sera agglutinated the cells of certain Rh positive genotypes other than those to which they belonged. These cases illustrate the importance of a complete examination of both cells and sera in all cases in which Rh investigation is undertaken.

In 2 cases of hydrops we had the opportunity of testing the serum for antibody at intervals during pregnancy.

CASE 1.

Mrs. S., aged 27 years. Group O. Rh negative.

1st and 2nd children normal. 3rd child died of icterus gravis. 4th child died *in utero*. Born macerated at 38 weeks. 5th child hydrops foetalis, delivered at 33 weeks. 6th child hydrops foetalis, delivered at 29 weeks.

Blood examined during the 7th pregnancy at 17th and 20th weeks and on the 8th day after delivery of a foetus with hydrops. The results are as follows.

Rh Antibody Titre During Pregnancy in Case 1.

| Time { | 17th week | 20th week | 36th week | 8th day puerperium |
|----------------|-----------|-----------|-----------|--------------------|
| Antibody titre | 1/16 | Nil | Delivered | 1/512 |

CASE 2.

Mrs. M., aged 19 years. Group O. Rh negative.

1st baby icterus gravis, transfused with Rh negative blood and recovered. 2nd baby stillborn with hydrops.

Blood tested twice during the 1st puerperium and at intervals during the 2nd pregnancy and puerperium. The results are as follows.

Rh antibody Titre during pregnancy in Case 2.

| 1st pregnancy | | | 2nd pregnancy | | | | | | | |
|----------------|------------|----------|---------------|----------|----------|----------|----------|----------|----------|---------------------|
| Time { | Puerperium | | 5 weeks | 16 weeks | 20 weeks | 24 weeks | 30 weeks | 33 weeks | 34 weeks | 14th day puerperium |
| | 4th day | 18th day | | | | | | | | |
| Antibody titre | 1/64 | 1/512 | 1/512 | 1/512 | 1/32 | 1/32 | 1/32 | 1/32 | 1/32 | 1/1024 |

The interest of these 2 cases lies in the diminution of antibody during the latter part of pregnancy. We believe that it is evidence that in cases of haemolytic disease of the newborn the antibody is absorbed and used up by the foetus and that the actual quantity used is not sufficient to alter the titre of circulating antibody until the foetus reaches a certain size, apparently some time about the 20th week. If this is true then this diminution of antibody titre has prognostic significance. The mere finding of antibody during pregnancy does not prove that the foetus will necessarily suffer from haemolytic disease of the newborn, firstly, because the antibody may be residual from a previous pregnancy and the foetus may be Rh negative and therefore not affected, and secondly, because on rare occasions it has been observed that an Rh negative mother with Rh antibody (observed during the puerperium) may have an Rh positive baby which does not show any signs of haemolytic disease of the newborn. (Boorman, Dodd and Mollison.⁶) If, as we suppose, the diminution of antibody indicates its absorption by the foetus, then it presumably indicates that the baby will show haemolytic disease of the newborn.

In Table II we draw attention to the fact that in addition to the 53 cases of classical haemolytic disease of the newborn demonstrable Rh antibody had been found in 8 other cases. In all 8 the foetus died *in utero* at or shortly before term and was usually born macerated. Certain workers

(Javert,^{15, 17} Henderson,^{18, 19}) have suggested that there is a 4th variant of haemolytic disease of the newborn which takes this form and in which although, due to maceration, an excessive erythropoiesis cannot usually be demonstrated, there are signs of damage to the liver with fibrosis. Our findings strongly support this view and we would urge that the clinical entity "haemolytic disease of the newborn" should in future be used to cover this 4th variant of its manifestations.

The histories of our 8 cases, which are summarized in Table III, were briefly as follows:

stillbirth. 6th stillbirth premature. 7th stillbirth full-time. 8th stillbirth full-time. 9th stillbirth full-time. 10th stillbirth premature. 11th stillbirth macerated. 12th pregnancy, tested at 28th week of pregnancy. Group O. Rh negative, antibody present. Unfortunately we were unable to retest the blood. Patient delivered of a macerated foetus.

CASE 3. (O.B., 27 years.)

1st pregnancy delivered at 3 weeks post mature stillbirth (cause unknown). 2nd pregnancy, full-time, stillbirth (cause unknown). 3rd pregnancy, tested at 33rd week. Group A₂. Rh negative, antibody titre 1/24.

34th week foetal movements ceased. 36th week delivered of a stillborn macerated foetus. Retested 1 week later, antibody titre 1/512.

TABLE III.

| Case | Age | Group | Antibody | Pregnancies | | | | | |
|------|-----|--------------------|----------|------------------|-----------------|-----------------------|------------------|--------------------|--------------------|
| | | | | 1 | 2 | 3 | 4 | 5 | 6 |
| 1 | 28 | A. Rh- | + | N | SB | SB | IUD | | |
| 2 | 42 | O. Rh- | + | (1) SB (7) SB | (2) N (8) SB | (3) Twins N (9) SB | (4) N (10) SB | (5) SB (11) IUD | (6) SB (12) IUD |
| 3 | 27 | A ₂ Rh- | + | SB | SB | IUD | | | |
| 4 | 33 | O. Rh- | + | Misc. | ND | ND | ND | IG | IUD |
| 5 | 28 | O. Rh- | + | N | ND | IUD | | | |
| 6 | ? | O. Rh- | + | N | N | IUD | | | |
| 7 | 35 | O. Rh- | + | N | IG | IUD | | | |
| 8 | 27 | A. Rh+ | + | N | N | IG | IUD | | |

N=Normal infant. SB=Stillbirth. IUD=Intrauterine death with macerated foetus.

ND=Neonatal death. IG=Icterus gravis.

CASE 1. (C.B., 28 years.)

1st child normal. Group A. Rh positive. 2nd child stillbirth (cause uncertain). 3rd child stillbirth (cause uncertain).

First tested at 8th week of 4th pregnancy. Group A. Rh negative, antibody titre 1/16. Retested 16th week of pregnancy, antibody titre 1/32. Retested 34th week of pregnancy, antibody titre 1/2. Foetal movements ceased at 36th week. Retested at 37th week, titre 1/16. Delivered at 37th week, of a macerated foetus. Retested during puerperium antibody titre 1/16.

CASE 2. (R.C., 42 years.)

1st child full-time stillbirth. 2nd child normal. 3rd twins normal. 4th child normal. 5th full-time

CASE 4. (Mrs. I., 33 years.)

1st pregnancy, miscarriage at 20th week. 2nd pregnancy, normal delivery. Neonatal death at 2nd day (cause unknown). 3rd pregnancy, labour induced at 28th week. Neonatal death (cause unknown). 4th pregnancy, labour induced at 28th week. Neonatal death (cause unknown). 5th pregnancy, labour induced at 32nd week, child showed icterus gravis but recovered (before the discovery of the Rh factor). 6th pregnancy, blood tested at 20th week. Group O. Rh negative. Antibody not demonstrated.

Retested at 30th week, antibody present in maternal serum only. 36th week delivered of a macerated foetus.

CASE 5. (Mrs. R., 28 years.)

1st pregnancy, normal child. 2nd pregnancy, neonatal death (probably haemorrhagic disease of newborn). 3rd pregnancy, blood tested at 26th week, Group O. Rh negative. Antibody titre 1/128.

Delivered at 36th week of a macerated foetus. Retested 6 weeks after delivery. Antibody titre 1/32.

CASE 6. (Mrs. R.)

1st pregnancy, normal child. 2nd pregnancy, normal child. 3rd pregnancy, delivered of a macerated foetus.

Blood tested at 10th day of puerperium. Group O. Rh negative, antibody titre 1/4.

CASE 7. (H.S., 35 years.)

1st pregnancy, normal child. 2nd pregnancy, child died of icterus gravis. 3rd pregnancy, intra-uterine death at 29th week.

Blood tested at 19th day of puerperium. Group O. Rh negative, antibody 1/128.

CASE 8. (E.F., 27 years.)

1st pregnancy, normal child. 2nd pregnancy, normal child. (Group A. Rh positive). 3rd pregnancy child died icterus gravis. 4th pregnancy, blood tested at 33rd week. Group A₂. Rh positive genotype either Rh⁺ rh or Rh⁺ Rh⁺. Rh antibody titre 1/2. Retested 36th week, antibody titre 1/4,000. Delivered 38th week of a macerated foetus. Retested 14th day of puerperium (about 18 days after death of foetus), titre 1/64.

It will be seen that in cases 4, 7 and 8 there was a history of haemolytic disease of the newborn in previous infants which, in view of the strong tendency of this disease to recur in each pregnancy, is evidence in favour of these cases being variants of haemolytic disease of the newborn. This view is also supported by a study of the antibody titres in 2 cases. In Case 1 it will be noted that the titre fell during the latter half of pregnancy and rose again after the death of the foetus, while in case 3, the titre rose after delivery.

If, as we believe, the low titre during the latter part of pregnancy indicated an ab-

sorption of antibody by the foetus, then it seems reasonable to suppose that the death of the foetus was associated with this absorption of antibody and that therefore the death was due to a form of haemolytic disease of the newborn.

Apart from these 61 cases of definite and supposed haemolytic disease of the newborn there were 10 cases of neonatal jaundice in which we were unable to demonstrate Rh antibody. In none of these cases was the clinical picture diagnostic of haemolytic disease of the newborn nor was there a significant degree of anaemia. We believe that they were cases of physiological jaundice.

In the remaining 209 cases in which Rh antibody was not demonstrable, the patients gave histories of a variety of obstetric mishaps, the 6 main ones being repeated abortions, unexplained stillbirths, unexplained neonatal deaths, congenital abnormalities, haemorrhagic disease of the newborn and toxæmias of pregnancy. It is difficult to classify these cases fully because many patients give a history of more than one condition but the number of patients giving a history of each condition was as follows:

| | |
|---|-----------|
| 1. Repeated abortions (up to 8 times) | 112 cases |
| 2. Unexplained stillbirths | 103 cases |
| 3. Unexplained neonatal deaths | 47 cases |
| 4. Congenital abnormalities | 20 cases |
| 5. Haemorrhagic disease of the newborn | 4 cases |
| 6. Toxaemias of pregnancy | 16 cases |

Of these 209 cases, 26 (12.4 per cent) were Rh negative and 183 (87.6 per cent) were Rh positive. These figures are in fairly close agreement with Landsteiner and Wiener's¹ figures of 15 per cent and 85 per cent respectively for the general population. In all cases the serum was tested for Rh antibody irrespective of the Rh group of the cells and in the vast majority of cases

the tests were carried out at a time when antibody, if present, could be expected to be at about its maximum.

In our series a history of repeated abortions was the commonest reason for asking for an Rh investigation; the supposition being that if Rh antibody can cause death of the foetus at or near term it may also cause miscarriage at an earlier stage. In fact our evidence is all to the contrary. In no single instance did we find any Rh antibody present and we feel that a series of over 100 cases is sufficient to give this result reasonable significance. Furthermore, if there were any connexion between the Rh factor and repeated abortions one would expect to find a history of the latter in the true cases of haemolytic disease of the newborn: in fact among our 61 cases, 6 only had a history of one abortion each.

Unexplained stillbirths was the other common reason for asking for an Rh investigation. Here the problem of deciding whether such an investigation would be of value is more difficult. Haemolytic disease of the newborn can cause stillbirths by hydrops or, as we have shown, by causing intrauterine death of the foetus. In these cases the investigation will almost certainly show the presence of Rh antibody and confirm the diagnosis and in the latter type of case is likely to be especially helpful in forming a prognosis. Apart from these 2 types of case however we have found no evidence of any connexion between the Rh factor and stillbirths.

Forty-seven of our cases gave a history of unexplained neonatal deaths. These were cases in which death could not be attributed to either icterus gravis or haemolytic anaemia on clinical grounds but in which it was thought possible that the Rh factor might have been responsible in some other way. In none of these patients were we able to find any evidence of Rh antibody.

In the group of congenital abnormalities we had 20 patients, 5 of whom had given birth to 2 affected infants, that is 25 abnormal infants in all. The lesions were as follows:

| | |
|--------------------------|----------------|
| Anencephaly | 12 cases |
| Spinabifida | 6 cases |
| Hydrocephalus | 2 cases |
| Imperforate anus | 1 case |
| Cleft palate and harelip | 1 case |
| Hare lip | 1 case |
| Atresia of the duodenum | 1 case |
| Unknown | 1 case |
| | <hr/> 25 cases |

It will be seen that the lesions are nearly all major ones and it seems reasonable to assume that if the Rh factor were responsible, we should have encountered Rh antibody in at least some of the cases or that we should have found a high percentage of Rh negative mothers. Actually only 3 out of the 20 mothers were Rh negative (15 per cent) and none showed any antibody.

Of the remaining patients there were 4 with a history of infants suffering from haemorrhagic disease of the newborn and 16 with a history of toxæmia of pregnancy. None of these patients showed any demonstrable Rh antibody. It should be noted in this connexion that Javert¹ states that infants suffering from haemolytic disease of the newborn may bleed spontaneously but he makes a clear distinction between this and true haemorrhagic disease.

SUMMARY.

1. The Rh reactions of a series of 280 selected obstetrical cases are reported.
2. The results confirm those of previous workers in cases of hydrops foetalis, icterus gravis and haemolytic anaemia.
3. In 3 cases the titre of Rh antibody was tested during pregnancy and was

found to fall after about the 20th week: it is suggested that this is due to its absorption by the foetus and is a bad prognostic sign.

4. Rh antibody has been demonstrated in cases of death *in utero* (with expulsion of a macerated foetus): this confirms the belief of Henderson and Javert that this is a 4th manifestation of haemolytic disease of the newborn.

5. We have not found evidence to suggest there is any connexion between the Rh factor and any of the following: repeated abortions, congenital abnormalities, haemorrhagic disease of the newborn, toxæmias of pregnancy, and also repeated stillbirths and neonatal deaths other than those due to the 4 variants of haemolytic disease of the newborn.

We are greatly indebted to our many clinical colleagues for supplying us with case histories. We are also indebted to Dr. G. L. Taylor for his constant help with difficult problems, and to Professor T. B. Davie for his interest and criticism.

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Riboflavin Deficiency in Pregnancy

BY

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THE syndrome of riboflavin (Vit. B₂) deficiency in the human presents distinct clinical features. These are principally maceration and fissuring at the lips and angles of the mouth (cheilosis and angular stomatitis), glossitis, seborrheic accumulations of the naso-labial folds, and certain ocular manifestations. The symptoms can be produced experimentally by the use of a diet deficient in riboflavin^{1, 2, 3}.

Experiments with animals as well as clinical observations lead to the belief that vitamin deficiencies during pregnancy may cause serious disturbances in the mother, and that they may also effect the development of the foetus. Moore and Brodie⁴ observed that female rats kept on a synthetic diet deficient in vitamin B complex frequently abort and resorb their foetuses. A significant relation between prenatal diet, course of pregnancy, and condition of the foetus on delivery has been found by Burke and collaborators⁵. Their study indicates that with inadequate nutrition during pregnancy there is increased incidence of complications and a larger proportion of infants in poor physical condition. A similar study by Ebbs⁶ and co-workers showed that malnutrition during pregnancy may lead to serious complications in both the mother

and the newborn. The incidence of miscarriages and premature births was found to be increased in women whose diet was poor. Quantitative studies of the vitamin B₁ requirements showed that the thiamine requirements during pregnancy are 3 to 5 times as high as in non-pregnant women (Toverud,⁷ Lockhart⁸).

It has been seen that pregnancy can also often reveal latent deficiency diseases. Strauss and McDonald⁹ have reported cases of sub-clinical vitamin B₁ deficiency, which became clinically manifest during pregnancy. Other reports¹⁰ as well stress the importance of pregnancy in the manifestation of deficiency diseases.

The present paper deals with the manifestations of riboflavin deficiency during pregnancy. In Palestine they are observed with some frequency in pregnant women. The disturbances occur almost always in women of poor economic circumstances. The patients complain of pain, of a burning sensation of the tongue, and of annoying burning in the upper part of the oesophagus. These and other signs of riboflavin deficiency become apparent during the second half of gestation and regress generally shortly after delivery.

The manifestations of riboflavin deficiency were noted in 21 per cent (190) of cases in a series of 900 pregnant women studied.

* Riboflavin is a necessary constituent of the diet; its richest sources are liver, brewer's yeast, milk, kidney, cheese, eggs, beef, ham, peas.

CLINICAL SYMPTOMS.

Glossitis: All studied cases (190) manifested glossitis in its various morphological forms. Papillitis (70 per cent), on the tip of the tongue or over its entire surface was the form most frequently observed (Fig. 1). Atrophic glossitis was noted in a large number of cases (25 per cent, Fig. 2). In 5 per cent of the observed cases the tongue showed severe ulcerative changes with desquamation of the lingual mucosa (Fig. 3). The colour of the tongue was purplish or scarlet red. The subjective complaints were pain and burning sensation in the tongue, particularly during ingestion of hot, acid or spiced foodstuffs.

Cheilosis: This symptom, well known as a specific sign of riboflavin deficiency¹, accompanied glossitis in 90 per cent of the cases.

Heartburn: A considerable number (85 per cent) of the patients suffered from severe heartburn. Most frequently the pharynx and the upper part of the oesophagus were involved. Intake of food sometimes caused painful sensations. Examination revealed in a great number of cases redness and atrophic changes of the visible pharyngeal mucosa. The heartburn seriously interfered with the ingestion of food, and thus aggravated further the existing condition of malnutrition. It should be emphasized that the heartburn was not relieved by alkali. In 22 cases an examination of the gastric juice was made. Normal values or slight hypoacidity were found.

Corneal vascularization: Of the entire group of 190 cases presenting signs of riboflavin deficiency, 91 women were examined with a slit lamp.* In 54 (60 per cent) corneal vascularization was found. This manifes-

tation has been claimed to be a specific sign of riboflavin deficiency^{2, 3}.

Other accompanying symptoms: In addition to aforescribed manifestations, other symptoms related to riboflavin deficiency were sometimes observed: (1) angular stomatitis in 44 per cent of the cases; (2) seborrheic accumulations on the naso-labial folds and around the eyes in 32 per cent of the cases; (3) vaginitis manifested by more or less abundant discharge and burning, occasionally accompanied by vulvar pruritus, in 28 per cent of the cases. This symptom is sometimes related to riboflavin deficiency (Sydenstricker^{11, 12}, Jeghers¹³).

Symptoms of other vitamin deficiencies were rarely observed: pellagrous dermatitis was found in 5 cases and neuritic manifestations in 17 cases. No clear-cut symptoms of vitamin C deficiency were seen.

CLINICAL COURSE.

All symptoms described above made their appearance almost simultaneously in the second half of pregnancy. Of the 190 cases only 24 were encountered in the first half of pregnancy. The greatest number occurred in the 6th month when 63 cases were registered. The frequency of appearance of the symptoms continued to be high in the 7th and 8th month, as may be seen in Chart I. The majority of manifestations regressed shortly after delivery; the subjective complaints, i.e. pain in the tongue and heartburn, disappeared in the 1st week after parturition. However, a longer time is required for the regression of the anatomical changes in the tongue following confinement. Cheilosis, angular stomatitis and papillary glossitis disappeared gradually during the 1st month following delivery, but atrophic glossitis and corneal vascularization rarely returned to normal even several months after

* We are indebted to Dr. B. Mitterstein and Dr. W. Kornblueth (Ophthalmological Department) for these examinations.

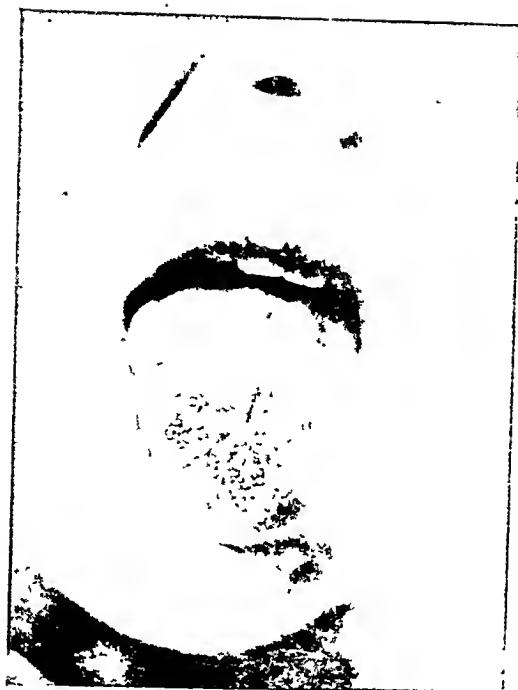


FIG. 1.

Papillitis spread over entire surface of tongue and cheilosis (6th month of pregnancy).

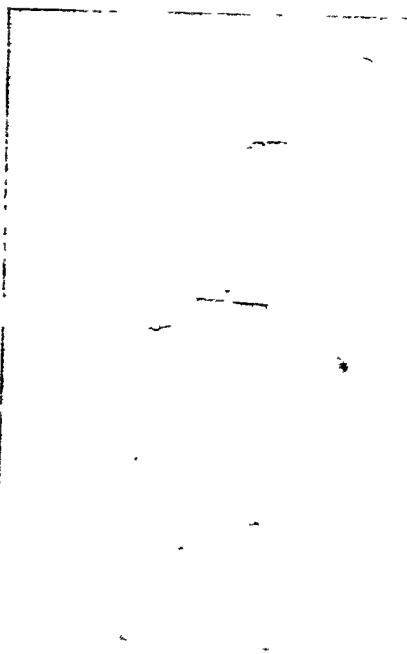


FIG. 2

Atrophic glossitis (6th month of pregnancy).



FIG. 3.

Desquamation of mucosa with ulceration accompanied by cheilosis (6th month of pregnancy).

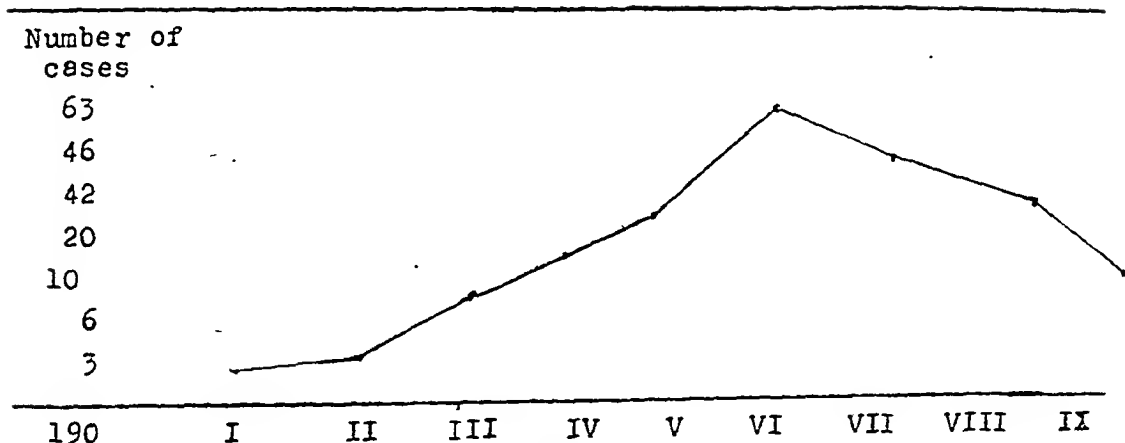


CHART I.

Curve showing the distribution of cases during the various months of pregnancy.

delivery despite the disappearance during the same time of the subjective complaints. Disappearance of symptoms of riboflavin deficiency was also observed following the death of the foetus *in utero*. In 2 cases relief of the complaints followed the death of the foetus *in utero* in the 8th month of pregnancy. It should be emphasized that a large number of the women studied in this series suffered from the described disturbances during successive pregnancies, but remained completely free from these symptoms in the intervals between their pregnancies. All these observations point to the existence of a close relation between the deficiency syndrome and development of the foetus.

LABORATORY TESTS.

The results of the laboratory tests* point, as do the clinical findings, to riboflavin deficiency as the aetiological factor. In 26 cases examined, definite diminution of riboflavin excretion in the urine was found.

The average amount of riboflavin excreted in the urine (determined by the method of Snell and Strong¹¹) was 95 gamma per litre in the patients, and 360 gamma per litre in a control series of normal pregnant women.

The majority of cases showed an anaemia of a normo- or hypochromic type. This may be regarded as a secondary symptom of malnutrition and iron deficiency.

ECONOMIC AND NUTRITIONAL DATA.

A detailed economic and dietary study was made of the entire group of cases. The study† leads to the conclusion that income in the greater part of our cases was below the minimal subsistence level (less than £.P 1.500 per head per month).

The diet of our patients was below the normal requirement and consisted principally of vegetables, fruits and carbohydrates. The protein intake was extremely low. This diet was particularly poor in

† A special report on this subject appeared in the "Inquiry into Poverty and Malnutrition Among the Jews of Jerusalem," published by the Hadassah Emergency Committee, Jerusalem, August 1943.

* The laboratory tests were performed by Miss Lea Bychowski, in the Department of Hygiene and Bacteriology, Hebrew University, directed by the late Prof. I. J. Kligler.

riboflavin. It has been found that the average daily intake of riboflavin in these women was less than 1.3 mg. This is far below the recommended level for pregnant women of 2.5 mg. (Committee on Foods and Nutrition, National Research Council.)

Therapeutical Assays: In 81 patients therapy with different components of vitamin B complex, and with an extract of yeast (Bevitex†) (see Table I) was attempted. Twenty-two women were treated with nicotinic acid, given in a dose of 300-500 mg. daily for 5 to 8 days. In 1 case only the subjective symptoms improved, but anatomical changes in the tongue and lips did not regress. Three women were treated with pyridoxine, each patient receiving 200 mg. No effect was observed.

In 30 cases an extract of vitamin B complex (Bevitex) was given for 7 days, the daily amount corresponding to 200-300 gram brewers yeast. Twenty-two cases were favourably influenced, in 8 cases an effect was not noted.

Thirty-three women were treated with riboflavin and striking effects were observed. Thirty-one of these responded favourably to riboflavin given in daily doses of 5 to 15 mg. by mouth for 3 to 7 days (7 of the patients had been previously treated with nicotinic acid without effect). Subjective complaints such as heartburn and pains in the tongue disappeared rapidly following treatment. With continued treatment regression of the anatomical lesions in the tongue and lips took place. The fact should be stressed that riboflavin was effective also in atrophic glossitis, a manifestation which is generally ascribed to nicotinic acid deficiency.¹¹ The relief of pains in the

tongue and the disappearance of heartburn permitted a painless and normal consumption of food. Institution of treatment was followed by rapid improvement of the general condition. The successful results of the riboflavin treatment thus give strong support to the assumption that ariboflavinosis is the aetiological factor in the manifestations which have been described.

COMMENT.

The outstanding features of riboflavin deficiency in pregnant women are glossitis and heartburn. Frequent accompanying symptoms are cheilosis, angular stomatitis and corneal vascularization. All these manifestations are regarded generally as characteristic of riboflavin deficiency. The greater number of our patients lived in poor economic circumstances and consumed a diet particularly low in riboflavin (the average daily intake being less than 1.5 mg.). The urinary excretion of riboflavin, determined in a number of cases, was found to be far below normal. Further proof of the aetiology of the syndrome was provided by the prompt curative effect of riboflavin therapy. In almost all cases the clinical symptoms made their appearance during the last trimester of pregnancy. This fact is explained by the increase in the nutritional requirements during this period. About two-thirds of the total gain in weight during pregnancy occurs in the last 3 months, because the foetus and its environment grow rapidly during this period. It is obvious that in women whose nutritional state is poor, the increase in nutrition required during pregnancy may lead to gross clinical deficiency. Confirmation of the rôle of gestation as a precipitating factor in the deficiency syndrome is found in the following observations:

(a) The patients did not manifest clinical deficiency symptoms prior to pregnancy;

† Riboflavin, nicotinic acid and Bevitex were kindly supplied by Assia, Chemical Laboratories Ltd., Tel-Aviv; Pyridoxin by Teva, Middle East Pharmaceutical and Chemical Works Co. Ltd., Jerusalem.

(b) The syndrome rapidly regressed after delivery or death of foetus *in utero*;

(c) The syndrome occurred frequently in successive pregnancies;

(d) The syndrome affects especially the pregnant member of the family, the normal members being less sensitive to riboflavin deficiency.

It has been claimed that an increased amount of oestrogenic hormone may favour the appearance of vitamin B deficiency.¹² If this claim is confirmed, it will follow that riboflavin deficiency during pregnancy may be due to the greatly increased production of oestrogens which normally occurs during pregnancy.

TABLE I.

Results of Treatment of Riboflavin Deficiency with Various B-Complex Vitamins.

| Treatment | Number of cases | Favourable results | No effect |
|---------------------------------|-----------------|--------------------|-----------|
| Nicotinic acid | 22 | 1 | 21 |
| Extract of yeast ("Bevitex") | 30 | 22 | 8 |
| Riboflavin | 33 | 31 | 2 |
| Pyridoxine | 3 | — | 3 |

SUMMARY.

(1) In a study of 900 pregnant women, 190 were found to suffer from a glossitis and heartburn. Often these symptoms were accompanied by cheilosis, angular stomatitis, and corneal vascularization.

(2) These symptoms made their appearance almost always during the last trimester of pregnancy and regressed shortly after delivery.

(3) An aetiological relation between

these symptoms and riboflavin deficiency was established by:

(a) Economic and dietary investigation,

(b) The low urinary excretion of riboflavin,

(c) The favourable response to treatment with riboflavin.

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"Long External Rotation" of the Foetal Head

BY

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MUCH has been written regarding the mechanism of internal rotation of the foetal head, but the mechanisms of restitution and of external rotation, which are usually simple and easily understood, are only briefly described in most text-books.

Once delivered, in occipito-anterior positions, the occiput moves through an angle of about 45 degrees towards the side to which it originally pointed. It thus assumes its original and normal position relative to the shoulders. Sometimes in occipito-posterior positions it moves backwards through 135 degrees in this movement of restitution, though this is not always seen because frequently the shoulders have already begun to rotate so that the back of the foetus is directed laterally. This type of restitution, which may be called "long restitution," is not always referred to in text-books, though Gibberd¹ describes it very clearly.

Thereafter follows the movement of external rotation. The anterior shoulder moves forwards and the head moves with the shoulders. In left occipito-anterior positions this means that the anterior shoulder moves from the mother's right towards her left until it reaches the midline, and the head moves with it through 45 degrees. The occiput now points directly to the mother's left, having undergone external rotation, a clockwise movement as viewed by the obstetrician. In left

occipito-posterior positions, after long restitution as described above, external rotation is an anti-clockwise movement of 45 degrees as the anterior shoulder moves 45 degrees forwards as far as the midline. It appears to be generally accepted, and stated in textbooks that both restitution and external rotation are movements in which the occiput moves to the side where it lay at the beginning of labour. While this is true of restitution, it is the object of this paper to show that occasionally external rotation may be in the opposite direction, so that the occiput may point to the side opposite to that towards which it pointed initially. De Lee² refers briefly to this and terms it super-rotation. This "long external rotation" can occur only as the result of the posterior shoulder instead of the anterior moving forwards towards the symphysis.

Whether we explain this by supposing the posterior shoulder first touches the pelvic floor, or whether we explain it by postulating different degrees of flexibility of the foetal trunk, need not be discussed here.

It is a useful practice to check one's diagnosis of the position of the foetal head by observing to which side external rotation takes place. Such a check is useful particularly when there has been some uncertainty of the position on account of a stout abdominal wall or a large caput

succedaneum which has obscured the fontanelles. There have, however, been occasions when I have felt certain of the position and yet external rotation has been to the opposite side. This may, indeed, lead to some embarrassment to a teacher who has announced that a case is left occipito-anterior and yet later on, at delivery, external rotation is to the right. In the words of De Lee: "The attendant will imagine his first diagnosis was wrong." Some of these cases may well have been the result of a misdiagnosis, but I have been suspicious for some time that long internal rotation of the shoulders as described above does in fact occur, and although it is not mentioned in the books I feel sure it must have been observed by many obstetricians. In delivery by the forceps, too, I have on occasion found external rotation taking place in the direction opposite to that expected, although with the patient anaesthetized there is usually little difficulty in determining the exact position of the head: until when, indeed, the forceps should not be applied. If it were left occipito-anterior I have on these occasions restituted the head to the left, but then found it necessary to move it swiftly to the right when, on pulling to bring down the shoulders, I have found the back coming out directly to the mother's right. Such cases always leave room for doubt whether one's diagnosis was correct, but a recent case has proved beyond doubt that this long external rotation of the head, due to long internal rotation of the shoulders, does occur.

The mother was a 2nd gravida, aged 30; the first delivery had been by the forceps. I had observed her regularly since her 2nd month of pregnancy and had found it necessary to perform external version for a breech presentation at the 30th week, again 4 days later, and once more at the 33rd week. After that the position was

always left occipito-anterior. When she came to delivery, I made a vaginal examination as soon as strong 2nd stage pains began: there was no caput succedaneum and the diagnosis of left occipito-anterior made by abdominal palpation was easily confirmed. The 2nd stage of labour lasted 45 minutes and was conducted in the dorsal position. Chloroform *à la reine* was administered as soon as the head appeared at the outlet. Internal rotation of the head was somewhat delayed: indeed the posterior fontanelle was still pointing several degrees to the left as the head was almost crowned, and it was necessary to rotate it deliberately to the midline to minimize the tension on the perineum, an easy procedure, of course, at this late stage. As soon as the head was delivered—there was no perineal tear—restitution occurred to the left, thus giving final proof that the position was in fact left occipito-anterior. The head was not touched at all except to wipe the eyes and to clear the throat, and it was left with the occiput pointing up towards the ceiling and to the left for some 2 or 3 minutes until the next uterine contraction occurred. The occiput at once returned to the midline and then continued to move in the same direction, anti-clockwise, until it pointed to the mother's right, thus rotating 135 degrees. Thereafter delivery proceeded as for a right occipito-anterior. In this case there was obviously long internal rotation of the shoulders; the movements were very easily observed since they occurred slowly on account of the very light chloroform anaesthesia.

I conclude, therefore, that although the direction of external rotation is usually a useful check upon the diagnosis of the position, yet it is not infallible. External rotation is not always to the side to which the occiput originally pointed, as is commonly stated. Long internal rotation of the shoulders may occur, so that the shoulders

may move through 135 degrees by the posterior shoulder instead of the anterior moving forwards towards the symphysis. If these events occur quickly, as they are particularly apt to do in a multipara (for the significance of which see below), the direction of restitution may escape notice, and the accoucheur may fail to appreciate that long internal rotation of the shoulders has taken place. If the delivery has been by the forceps under fairly deep anaesthesia, the accoucheur may himself restitute the head to the side which he thinks proper before pulling down the shoulders. If he should be inexperienced and if long internal rotation of the shoulders take place, he may not perceive what is happening and he may insist on turning the head to one side while the shoulders are turning to the other. The child's neck will then be subjected to considerable torsion.

Theoretically another variety of long external rotation of the head is possible. After "long restitution" in occipito-positions the posterior shoulder may undergo long internal rotation. In left occipito-posterior positions the movements of the occiput would then be: long restitution 135 degrees clockwise (i.e. to the mother's left) and then long external rotation for another 135 degrees in the same direction, so that it would point first to the mother's anus and finally to the mother's right thigh. This I have not hitherto observed.

How does it come about that the posterior shoulder reaches the pelvic floor before the anterior? In a private communication Professor Miles H. Phillips, to whom I wrote regarding this phenomenon, relates an explanation which Professor Chassar Moir advanced to him in discussing the matter. Professor Chassar Moir wrote: "I fancy the explanation is that the anterior shoulder may become hitched up on the pubic bone and so does not descend into

the pelvic cavity in alignment with the posterior shoulder. The obliquely placed posterior shoulder is then pushed right to the front (long rotation) and finally the shoulder that is hitched up on the pubic bone moves to one side and slips down in the normal manner." Professor Phillips directed my attention to William Smellie's advice to prevent the shoulders from hitching on the upper part of the os pubis or sacrum. It is to be found in the Sydenham edition, Volume 1, page 274 and also pages 272, 273 for McClintock's comments. I have not got this edition, but have access to the 1779 edition "printed for W. Strahan; T. Cadell, and G. Nicol, in the Strand; and W. Fox, and S. Hayes, in Holborn." In this edition the advice is to be found on pages 232, 233 as follows: "When the head is come low down, and cannot be brought farther, because one of the shoulders rests above the Os pubis, and the other upon the upper-part of the Sacrum, let the head be strongly grasped with the forceps, and pushed up as far as possible, moving from blade to blade as you push up, that the shoulders may be the more easily moved to the sides of the Pelvis, by turning the face or forehead a little towards one of them; then the forehead must be brought back again into the hollow of the Sacrum, and another effort made to deliver: but, should the difficulty remain, let the head be pushed up again, and turned to the other side; because it is uncertain which of the shoulders rests on the Os Pubis or Sacrum. Suppose, for example, the right shoulder of the child sticks above the Os pubis, the forehead being in the hollow of the Sacrum; in this case, if the forehead be turned to the right-hand side of the woman, the shoulder will not move; whereas if it be turned to the left, and the head at the same time pushed a little upwards, so as to raise and disengage the parts that were fixed, the right shoulder being towards the right-

hand side, and the other to the left side of the brim of the Pelvis, when the forehead is turned back again into the hollow of the Sacrum, the obstacle will be removed, and the head be more easily delivered."

This point receives little attention nowadays. Smellie evidently regarded internal rotation of the head as important in producing a proper movement of the shoulders to enable them to descend easily. If the shoulders stuck, he produced super-rotation of the head by the forceps in order to make them clear the pubis or sacrum and descend. It seems clear that the example he gave, quoted above, was a left occipito-anterior. Now Windemeyer and F. J. Browne³ have emphasized that the anterior shoulder lies some distance from the midline in occipito-posterior positions, and it therefore seems likely that the anterior shoulder would less frequently be caught by the pubis in such positions than in occipito-anterior positions, in which the anterior shoulder lies nearer to the midline. If this is so, and Chassar Moir's suggestion is correct, then long external rotation of the head in occipito-posterior positions, which, as I

have stated above, I have not yet seen, would be equally rare. Finally, one would expect a shoulder to be more readily caught by the pubis in multiparae with flaccid abdominal walls, and they should therefore exhibit long external rotation of the foetal head more frequently than do primigravidae and women with strong abdominal walls. Further observations upon these points may prove interesting.

I wish to offer my grateful thanks to Professor Miles H. Phillips for his valuable criticism of this paper and for pointing out to me Smellie's observations; also to Professor Chassar Moir for the explanation he has offered and which is mentioned above.

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External Endometriosis and Pregnancy (Report of Two Cases)

BY

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THE increasing practice of microscopic study of gynaecological material has thrown more light on the condition of endometriosis. While all statistics agree on the great frequency of sterility in cases of endometriosis,^{1, 2, 3, 4}—Dreyfuss⁵ gives 31 per cent and Counseller⁶ 32.1 per cent—there is an increasing literature dealing with the association of pregnancy and endometriosis. An excellent review of the subject has recently been made by Scott⁷ who added 2 cases of his own.

For clarity, endometriosis is described as internal and external. In the first type the condition is limited to the uterine musculature while the external type includes all other areas containing ectopic endometrial tissue. The two conditions cause different complications in pregnancy, and external endometriosis is more commonly associated with sterility.

Of the 2 cases to be presented the first is one of ovarian cyst of endometrial origin discovered on routine examination at the first visit to the antenatal clinic, while the second is far more unusual, being the only case of tubal endometriosis associated with an intra-uterine pregnancy reported in the literature available at present, which has been limited owing to wartime conditions.

CASE 1.

Mrs. E.M.F. Married; age 30. No previous pregnancies.

History. First seen April 17th, 1944. L.M.P.

February 4th, 1944. Periods previously lasted 6 to 7 days and occurred every 28 days. Loss heavy, slight dysmenorrhoea. Bowels regular, slight urinary frequency for 2 months. No previous illnesses or operations.

On examination. Healthy woman, heart and chest normal, blood-pressure 130/70.

Urine: Acid, no abnormal constituents present. There was a mass in the right iliac fossa the size of an orange.

Per vaginam. Vulva and vagina normal. Cervix healthy and slightly softened. Uterus enlarged to the size of an 8 weeks' pregnancy pushed back by a cystic mass the size of a navel orange lying in front and to the right of the uterus and continuous with the mass felt in the abdomen.

Provisional diagnosis. Right ovarian cyst and pregnancy.

Operation: May 26th, 1944. *Findings:* The uterus was the seat of a 14 weeks' pregnancy. There was an ovarian cyst the size of a navel orange lying in the right paracolic gutter behind the uterus. *Procedure:* Right oophorectomy.

Convalescence: Normal. The patient was well sedated and given intramuscular injections of luto cyclin. She was discharged to attend the antenatal clinic; the pregnancy continuing.

Pathology: The ovarian cyst contained a quantity of chocolate substance. It measured approximately 6 x 6 cm. in its collapsed state.

The section of the ovary is that of a chocolate cyst with a most conspicuous decidual reaction.

Comment: According to Scott⁷ the ovary is the second most common site for external endometriosis complicating pregnancy. He found in his review of the literature that endometriosis of the recto-vaginal septum, although not so common as ovarian endometriosis, more frequently caused symptoms



FIG. 1.

Microphotograph of section of wall of the ovarian cyst removed from Case 1. The right half shows the ovarian stroma while the left half consists of endometrial glands embedded in a stroma which has undergone a decidual reaction.



FIG. 2.

Microphotograph of a section of the tube removed from Case 2. The section shows the tubal epithelium lining the lumen and in the wall of the tube an endometrial gland surrounded by endometrial stroma which has undergone a decidual reaction.

seen and no attempt was made to inspect the left Fallopian tube and ovary or the pouch of Douglas to avoid excessive handling of the pregnant uterus.

Pathology: The specimen consisted of a Fallopian tube and ovary, the former enlarged in the ampullary portion by a tumour the size of a golf ball. The ovary was the seat of a corpus luteum of pregnancy. Sections of the ovary revealed a well-developed corpus luteum of pregnancy. Sections of the tumour of the Fallopian tube at first revealed the tubal lumen lined by normal tube epithelium and in the wall a mass of decidual cells lying in the muscular coat. Further sections revealed endometrial glands surrounded by decidual cells embedded in the muscular coat.

Sections of the macroscopically normal Fallopian tube showed similar changes.

Convalescence: The patient was well sedated and given intra-muscular injections of lipo-lutein. At the end of 17 days she developed a B. coli cystitis which subsided on treatment with sulphonamides. The urine became sterile on culture and the patient was discharged on March 3rd, 1943.

Labour: Began on July 7th, 1943, and was normal. She was delivered of a living male infant 6 pounds, 1½ ounces.

Post-natal examination: September 8th, 1943.

Comment: As several sections of the Loop y material were necessary to establish the diagnosis, an attempt was made to review the literature on the subject.

Endometriosis of the Fallopian tube has been noted more frequently of late, " " " ".

Provisional diagnosis: Right ovarian tumour and probable pregnancy.

Procedure: An attempt was made to resect the Fallopian tube and leave the ovary as it contained the corpus luteum of pregnancy, but haemorrhage was difficult to control, so a right salpingo-oophorectomy was performed. The appendix was not

Haydon⁴ reviewed a series of 569 cases of endometriosis and found that in 16 (2.8 per cent) the lesion was in the Fallopian tube. Emphasis has been laid on the involvement of the tubal epithelium. Frankel and Schenck⁸ consider that ectopic endometrium in the Fallopian tube is the cause of ectopic gestation. Their evidence is based on the study of serial sections of Fallopian tubes removed for ectopic pregnancy and they noted chiefly changes in the tubal epithelium or endometrial tissue in the tubal lumen which had undergone a decidual reaction. They report 1 case in which endometrial tissue was found at the abdominal end of the Fallopian tube and another in which the tissue was seen at the junction of the ampullary and infundibular portions and they quote a case of Hohne in which the endometrial change was found in the intramural portion of the Fallopian tube. Marchetti⁹ reported 2 cases in which lining of the tube was replaced by endometrium. The change in both cases involved the distal two-thirds of the tube. Both patients had previously borne living children but neither was pregnant at the time when the condition was observed.

Philipp and Huber¹¹ consider that adenomyosis occurs chiefly in the interstitial portion of the Fallopian tube and is extremely rare in the more lateral areas. They state also that in more than 20,000 serial sections there was a continuation with the corporeal endometrium, and they compare the condition to adenomyosis uteri interna with the proviso that in the latter condition the endometrium permeates deeply into the myometrium, whereas in the former the spread is lateral, the transitional area between uterine and tubal mucosa being pushed further and further outwards.

This case presents several features of interest:

1) It is the only case of tubal endo-

metriosis and intrauterine pregnancy which the author has been able to trace.

(2) The site of the tubal involvement was unusual, the muscular coat and not the epithelium being involved.

(3) The ampullary portion of the tube was attacked and not the more usual interstitial area.

(4) The diagnosis was incorrect. This was so in most cases of uterine pregnancy and endometriosis reported in the literature. At first on the microscopic report one was inclined to think that the condition was one of intra- and extrauterine (tubal) pregnancy.

(5) That pregnancy occurred and implantation was in the uterus can probably be explained by the fact that the area affected was the tubal muscular layer and not the epithelium. A lesion in the tubal epithelium usually causes partial or complete blocking of the lumen, a condition which would favour ectopic gestation or sterility. The possibility of external migration of the ovum, however, must not be forgotten.

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Some Curiosities of Mammalian Reproduction

Part 3.—Mammals that Produce Uniovular Litters *

BY

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A curious phenomenon has long been known by entomologists to be displayed by certain parasitic Hymenoptera. This phenomenon was first investigated by Silvestri. He found that "in the genus *Litomastix*, in which the eggs are laid in the body of a caterpillar, a single egg divides very early into a large number of separate embryonic primordia, each of which produces an adult insect. No matter how many individuals are derived from one egg—the numbers may be even a thousand—they are of the same sex." No mammal can claim any achievement so dramatic as this but some of them have succeeded in producing some rather astonishing results in the direction of begetting uniovular litters.

MAMMALS THAT HAVE HAD TO REDUCE THE SIZE OF THE FAMILY.

THERE have been many theories put forward to account for the fact that some mammals produce large litters and have large families while some have only small ones.

Herbert Spencer (1899) had a theory. "According to this theory the power to sustain individual life and the power to produce new individuals are inversely proportional, a conclusion which is summarized in the generalization that Individuation and Genesis vary inversely."

F. H. A. Marshall (1922) has also formulated a theory. "Broadly speaking, the average number of young produced in a litter in any species of mammal is inversely proportional to the average size of the animals belonging to that species." In homely language, these two theories postulate alternatively:

(a) that long-lived mammals have smaller families than short-lived ones, and

(b) that big mammals have smaller families than little ones. But neither of them taken separately nor both of them considered together would seem to provide a very satisfactory solution of the business. Indeed it would be very interesting to learn the opinion of the Shrew concerning Spencer's dictum. For a Shrew, born in May or June, is dead before its second Christmas Day comes round. In its short life, it may perhaps produce two litters. What then would the Shrew say when it learned of the elderly female Rabbit, perhaps a dozen years old, that had regularly produced litters of five or so several times a year? It would be equally interesting to know what that tiny mammal, a Pipistrell bat, would think of Marshall's theory. For the Pipistrell produces only one offspring once a year and so would feel dissatisfied with the dicta of science when it considered the case of the bulky sow, followed at frequent periods by recurrent and ample litters of piglets. Probably neither the Shrew nor the Bat would consider the theories entirely satisfactory or of very general application.

At the present moment there are, I believe, committees appointed by the Government and composed of especially gifted and eminent persons, considering the question of increasing the birth-rate when this

* Lloyd Roberts Lecture—Part 3.

war is over. The following quotation is taken from an Arris and Gale Lecture delivered during the European war of 1914-18. It was written without regard to human problems. "*Large families can therefore only be indulged in, as a rule, by animals the females of which may be exempted from any very exacting activity during pregnancy.*" Such is a general axiom among the mammals and, leaving altogether the stock with which we are most concerned, examples of its truth are readily furnished in many Orders. Herbert Spencer gave much thought to the well-known instance of the relative fertility of the hare and the rabbit. Much of his speculation was no doubt true; but we must not overlook the fact that a doe rabbit's home is safe in a burrow, while the female hare has no such protection, and the same cause that has led to the reduction of the hare's litter has been at work, with even greater force, among the Ungulates. Again, in aquatic life the same disability is felt and the picture of the pelagic life of the whales makes the second axiom—that, *where there is no nursery there will be no large families—more real.*" This was written as part of an essay that attempted to outline "The Influence of the Arboreal Habit in the Evolution of the Reproductive System." The thesis it sustained was that since a female animal that lived a truly arboreal life was severely handicapped in its activities when pregnant of a large litter and could not nurse helpless young in the tree tops, the Primates had tended to reduce the number of young produced at a birth and so limited the size of the family. Perhaps the thesis may be extended from the Primates as an interesting mammalian phylum in general, to Man, one of the more interesting members of the phylum, in particular. It may be that the gifted scientists and others, who are now planning for the post-war increase in the num-

ber of births, would do well to bear in mind these two axioms: (1) Mammalian females, if they are to produce large families, must be "exempted from any very exacting activity during pregnancy" and (2) they must be provided with a safe retreat and a satisfactory nursery before much can be expected from them in the way of producing the large families that the statesmen appear to think so desirable at the moment.

There is a type of writer, who in certain literary activities impinges on biological subjects, and who never tires of telling us of the prodigality with which Nature produces a vast excess of offspring; an excess that can never hope to attain to maturity or even to enjoy life at all. I do not think it requires great erudition to detect the underlying implications that attract some people to such a view of the workings of Nature. Were there no excess of offspring to be weeded out what would happen to the fundamental teaching of the Struggle for Existence? What would become of the Doctrine of the Survival of the Fittest? Surely we must have Nature red in tooth and claw else the redness of our own talons might be deemed as something not quite in harmony with the ways of Nature!

Perhaps as a corrective to this rather fashionable mode of thought concerning the wasteful way in which Nature permits offspring to be born only to be eliminated in bitter and bloody struggle, it may be well to consider the converse of the problem. Most assuredly there is another side to the picture, for nothing is more striking in the story of mammalian reproduction than the harmonious adaptation of structure and function to limit the number of offspring produced by those mammals whose habits and environment prevent them from having access to a natural nursery in which the offspring may be tended by the mother.

It is easy to picture the outstanding

factors of environment and habit that deprive the mammalian mother of a natural nursery. If the mother lives in the tree tops she can neither be pregnant with a large litter nor deal with a large number of helpless offspring when born. Mammalian nest building though a widespread habit with arboreal marsupials, rodents and primates, does not solve the problem for animals of any considerable size. Arboreal American opossums (*Didelphis*, etc.) and Australian arboreal phalangers (*Trichosurus*, etc.) may overcome the difficulty by resorting to such expedients as intertwining prehensile tails or carrying the young in a pouch; but these things are no more than makeshifts at the best. The arboreal primates and arboreal edentates have solved the problem by reduction of the number of offspring produced at a birth.

Again if a mammal leads a completely pelagic life the mother finds no nursery and all the Cetacea have had to limit the litter to single births. Defenceless animals that live in open spaces and have to seek safety in instant flight in the face of danger are in the same case and many cursorial ungulates, rodents and marsupials cannot afford to be pregnant of or to beget multiple offspring. And lastly, volant animals, like the bats, that must needs carry the helpless young with them as they fly in search of food, have come under the ban of prohibition and have to be content with one or perhaps two at a birth.

It is only the strong and the well-armed, or such of the weak and defenceless as happen to have homes and safe retreats in lairs or holes or burrows or nests that can afford large litters that they may nurse and tend in safety and at their leisure.

Now if circumstances of habit and environment dictate that the number of offspring produced at a birth should be only one or perhaps two, that the mother

may nurse and defend, several anatomical and functional changes must be brought about.

In the first place, it is obvious that the number of ova shed at any period of ovulation must be reduced. If multiple ova are passed into the female passages at any act of ovulation their fertilization is guaranteed, for there is no reduction in the vast number of spermatozoa awaiting them.

Next, it is necessary that a definite single-pregnancy type of uterus should be reshaped from the common mammalian multiple-pregnancy type. And lastly, since a full series of mammary glands is no longer necessary, there will be reduction in their number.

It is apparent that the mammals producing single offspring, including such diverse forms as some primates and edentates, most cetacea, certain ungulates and rodents and the bats, have no phylogenetic or taxonomic affinity. They constitute, in this connexion, a group of animals bound together by a single functional bond. They are animals that, because of habit and environment, have had to reduce the typical mammalian litter to the production of a single offspring at a birth. It is this plain physiological fact that renders the striking similarity of their structural and functional adaptation so instructive. Changes are effected harmoniously in the ovary, the female reproductive tract and in the mammary system. Here the changes brought about in these three systems can be reviewed only briefly.

The primitive mammal was almost certainly endowed with multiple functional mammary glands and nipples. All the primitive non-arboreal insectivora possess a full series. The tenrec of Madagascar (*Centetes caudatus*) has no less than 11 pairs of mammary glands and nipples and litters as large as 21 have been recorded.

In all the typical primates the functional

mammary glands have been reduced to a single pair, pectoral in their position. In such edentates as the sloths and anteaters only one pair of pectoral mammae is present. In the perissodactyle ungulates the single pair is typically inguinal in position, as is the reduced series of single-offspring cursorial rodents. The mammary glands of the pelagic whales and dolphins are also reduced to a single pair and these glands are situated on either side of the vulva. The volant bats again select a pectoral site for the single pair of functional mammae retained. The general principles involved in the business may be summed up by saying that if any mammal, no matter what its phylogenetic status may be, has, by habit or environment, to adopt single-offspring pregnancy, the series of mammary glands will be reduced to a single functional pair and their site will be that dictated by the mother's convenience in nursing. No mammal has so far transgressed, nor is likely to transgress, the great law of general bilateral symmetry as to reduce the mammary series to a single unit.

As for the necessary modification of the primitive mammalian reproductive duct system, it is remarkable how similar are the stages rehearsed by all single-offspring mammals and how strikingly similar are the end results produced despite any sort of phylogenetic kinship.

In the whole course of the female genital ducts (Müllerian ducts) there are, in the embryos of all mammals, three very distinct portions separated by definite landmarks. The most cephalic portion of the ducts stretches from the abdominal ostium to the point at which the gubernacular strand of the ovary (round ligament) crosses the duct. This cephalic part lies primitively in the long axis of the body and is destined to become the so-called Fallopian tube. The next part is embraced between the point of attachment of the gubernacular strand and the

place at which the two ducts of the opposite sides of the body become approximated in the midline and enveloped in the tissues of the "genital cord." This is the part that tends to lie transverse to the long axis of the body and it forms the uterine cornua of the adult. The last part, confined in the genital cord, fuses with its fellow of the opposite side and forms a single median chamber—the corpus uteri (See Fig. 19).

The most distal sections of the female ducts (Fallopian tubes) are destined to become the true oviducts in all mammals, for they convey the ova from the ovaries to the pregnancy chamber. The middle portions, in the typical mammals that produce multiple young at a birth, become the bilateral pregnancy chambers or cornua uteri. The terminal median portion becomes the common passage through which the foetuses leave the uterus for the vaginal canal at birth (See Fig. 20). Since in the mammal that produces only a single foetus at a pregnancy the long double pregnancy chambers cease to be necessary they undergo a steady reduction in the stages of ontogeny. This shrinkage is marked by the increasing approximation of the point of attachment of the gubernacular strand and the corpus uteri itself. In the end the two cornua shrink inwards towards the corpus uteri to such an extent that they cease to exist as entities and the gubernacular strand becomes attached to the sides of the corpus uteri itself. With the diminution of the cornua the corpus uteri enlarges to form the single pregnancy chamber destined to be the place for the foetus (See Fig. 21).

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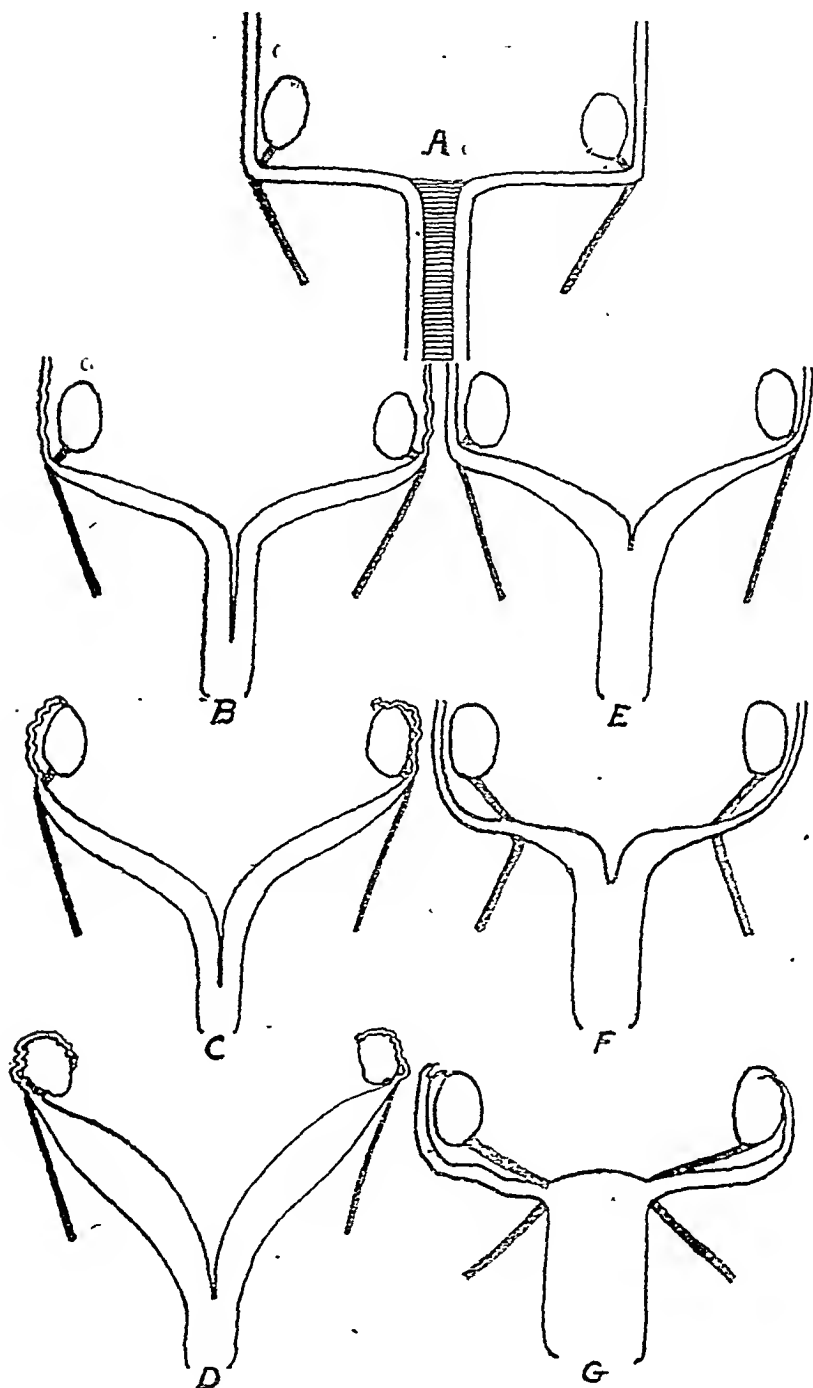


FIG. 19.

Developmental stages of (B.C.D.) the multiple-pregnancy and (E.F.G.) single-pregnancy type of uterus from the primitive condition shown in A.

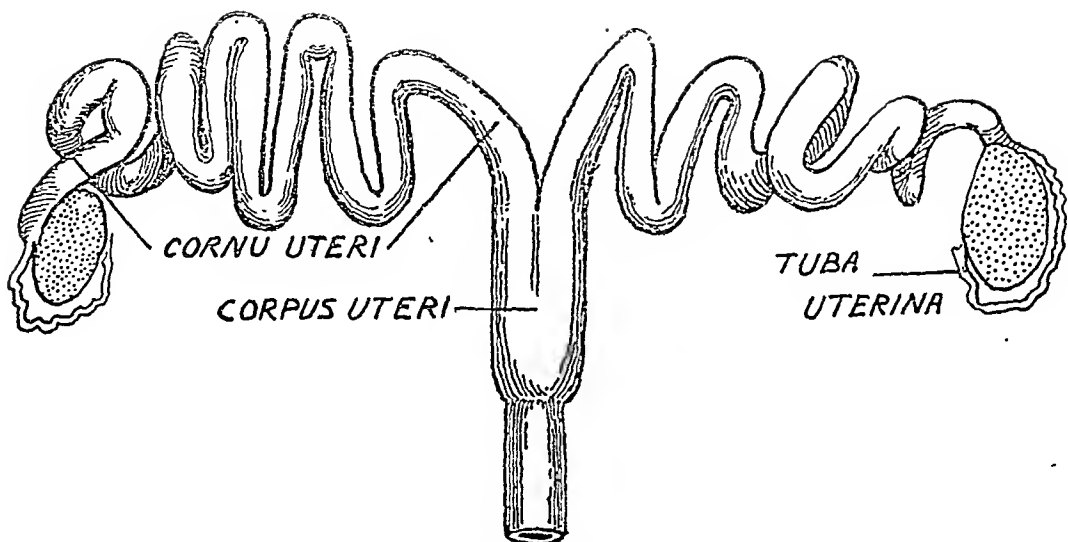


FIG. 20.

The multiple-pregnancy type of uterus, with large cornua, small body and minute tubes. The uterus is that of a sow.

delimit the Fallopian tube segments from the corpus uteri segment and the round ligament of the ovary and the round ligament of the uterus, instead of being in a direct

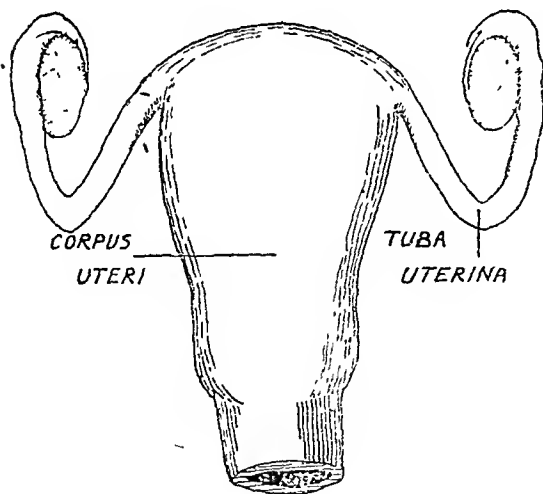


FIG. 21.

The single-pregnancy type of uterus, with large body and tubes but no cornua. The uterus is that of Homo.

line are at an acute angle to each other—the angle being formed by the complete regression of the cornua uteri into the corpus uteri. The cornua have disappeared, not by fusion to form the large corpus uteri as is often assumed by human anatomists, but by shrinkage towards the corpus uteri. If any portions of the typical mammalian cornua persist in the corpus uteri of the single-offspring mammals, they are to be looked for in the short pars uterina tubae.

When we come to seek for facts regarding the changes in the ovary whereby a reduction of the number of ova shed at a period of ovulation is brought about, we have no such satisfactory basis for assurance as we have in the case of the mammary system or in that of the female genital ducts. There are not sufficient facts recorded to enable us to write a history of the structural and functional changes in the ovary that ultimately lead to the production of only a single ovum at the time of the ovulation. Strangely enough it is only concerning two of the more outlandish

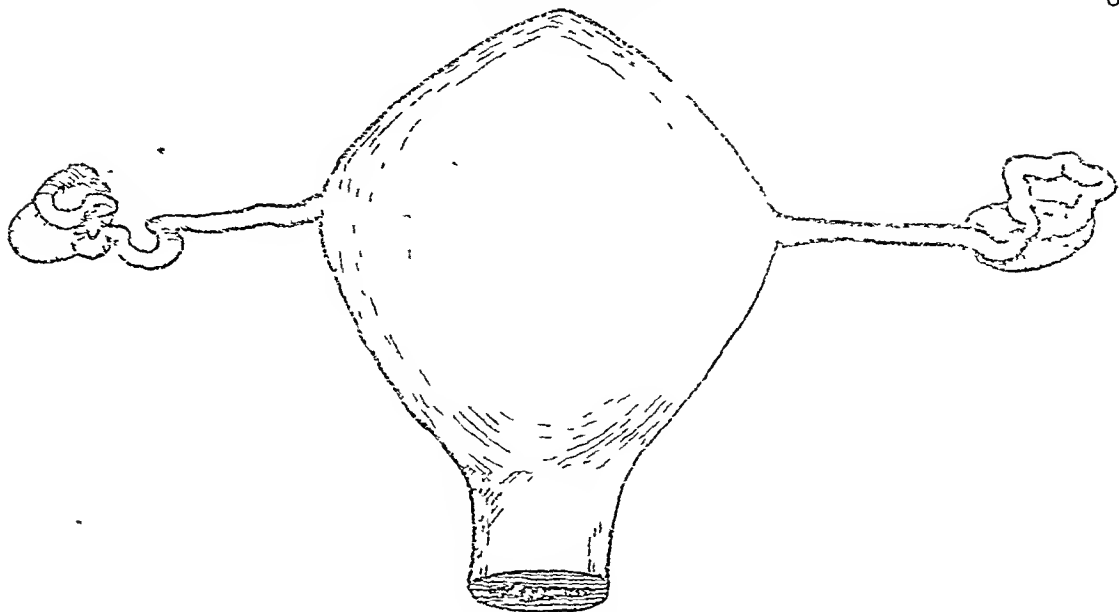


FIG. 22

The single-pregnancy type of uterus of an armadillo

(After Newman)

members of the single-ovum mammals—armadillos and bats—that we have any really definite knowledge. We cannot hope

for a series of overt demonstrations of the actual number of ova shed from the ovaries during the period of ovulation in a wide series of mammalian types. But fortunately a visible record always persists of the actual shedding of the ovum. The bulky corpus luteum is always to be found in the ovarian follicle from which the ovum was shed. (See Fig. 24.) It is therefore necessary to rely upon the findings as to the number of corpora lutea present in the ovaries of pregnant animals in order to estimate the number of ova shed from the ovary during the period of ovulation. Fortunately in the case of at least 2 mammals we have direct evidence that the production of ova has been reduced and that only one is normally produced to become fertilized and so to provide the basis of the ensuing pregnancy.

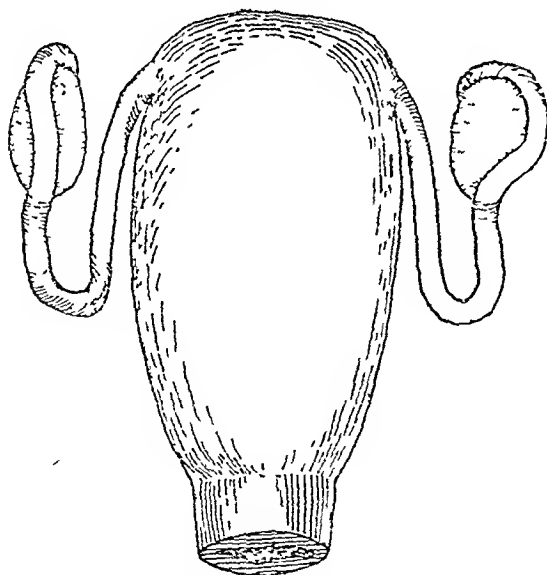


FIG. 23

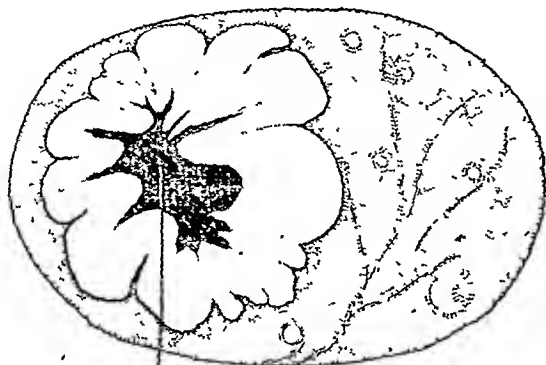
The single-pregnancy type of uterus of a phyllostomid bat.

(After Robin)

THE REPRODUCTION OF THE EDENTATES.

The edentates are, as a group, no great favourites with the systematic mammalo-

gist for they do not fit very readily into his orderly schemes of classification. Certain characters are common to them all, but many of these common characters are such as might be expected to distinguish the existing members of almost any stock that



CORPUS LUTEUM

FIG. 24.

Outline drawing of a section of an ovary to show the single corpus luteum of pregnancy

has fallen out of the race for progress and has become phylogenetically senile. Specialized diet, specialized habit and specialized anatomical developments distinguish them all and of all of their specializations it may be said that they are such as lead to nowhere in the mammalian march of progress. Perhaps it is for this very reason—that they are possibly a mammalian job lot—that they are of most interest to us in connection with their reproductive story. Most probably all the members of the Order that inhabit the New World are bound together by real, if not very immediate, bonds of affinity and fortunately we have every assurance that the group of the armadillos, with which we are more especially concerned, are all near akin.

One very definite specialization that the sloths, the anteaters and the armadillos of the New World have all embarked upon is the development of a simple, globular

single-pregnancy type of uterus and a reduced series of mammary glands and nipples. Quite obviously, from the point of view of the relation of structure to function, they have all carried out all the anatomical changes that are characteristic of mammals that have reduced the size of the litter. Apparently no detailed accounts of the whole reproductive history of the sloths (*Bradypodidae*) or of the anteaters (*Myrmecophagidae*) have been published. We do, however, know that among the sloths a typical single-pregnancy uterus and a mammary series reduced to a single pectoral pair of glands and nipples have been uniformly achieved. The same generalization holds good with the anteaters and, in the absence of any evidence to the contrary, we may assume that in all of them only one offspring is produced at a birth, as is the case with those few species concerning which there is any definite information.

It is only concerning the reproduction of certain species of armadillos that all the essential facts are definitely known and extremely strange facts they are. Although it is so long ago as 1885 that the curious story was first told, more than a quarter of a century elapsed before renewed scientific researches made it impossible to ignore or to disbelieve in the occurrence of the strange happenings that H. von Jhering had first claimed to be realities.

Von Jhering had examined 2 pregnant females of the species known as *Tatusia hybrida* that inhabits Argentina and whose local vernacular name is Mulita. He found in the simple uteri of both these females no less than eight embryos and these embryos were all enclosed within one chorionic membrane. More than this, all the embryos of both females were of the same sex, for both sets consisted entirely of males. The facts of this original finding were published as a brief note in 1885 and

in the next year the case was reviewed in another communication and now the almost unavoidable conclusion was arrived at—that each of these sets of 8 identical, same-sexed embryos had been derived from a single fertilized ovum. Von Jhering postulated the almost unbelievable, yet almost inescapable thesis that the entire litter of 8 embryos of *T. hybrida* had somehow been derived from the subdivision of a single ovum into 8 separate and identical individuals. Unfortunately, and owing to a stupid mischance, this strange finding did not receive the attention it deserved. Von Jhering had sent the ovaries of a female armadillo of another species (*T. novemcincta*) of the same genus to Rosner for examination and in 1901 an account of the microscopical structure of these ovaries was published. In this paper Rosner claimed that the only thing that was strange about the business was that the ripe ovarian follicles of this animal frequently contained multiple ova. According to Rosner's finding, all that happened was that the rupture of an ovarian follicle in the act of ovulation released many separate ova instead of the usual one and that the embryos present in the uterus were the products of separate ova in the manner usual among mammals producing multiple offspring. It therefore became accepted that the separate ova instead of having come from an equal number of separate follicles had in the case of this animal been matured within and released from a single follicle, but otherwise the process of reproduction was normal. Although this account of the process as given by Rosner entirely overlooked the outstanding fact that all the embryos in both litters were of the same sex, it appeared to fit into the general body of knowledge of the formation of multiple pregnancies of lower mammals and as a consequence the interest in the peculiar reproductive habits of the arma-

dillos lapsed for a time. It was not until 1909 that M. Fernandez re-examined the embryological history of *T. hybrida*. His researches revealed the fact that though 8 embryos constitute the usual litter, the number of young produced at a birth varied from 7 to 12. But he also showed quite conclusively that only 1 ovarian follicle, containing 1 ovum, and, subsequently, a single corpus luteum was involved in any individual pregnancy. Moreover, he made a thorough examination of the early stages of embryonic development and showed how the embryonic rudiment of the original single blastoderm vesicle underwent a process of fission. The ectoderm of the embryonic plate produces outgrowths from its central area and these outgrowths become in their turn areas of growth and development which, by extending away from the central area, form the bases of independent embryonic differentiation. At first, the embryonic area gives rise to two outgrowths at opposite sides of the little disc of cells. Next, two more are produced on an axis at right angles to that of the first two. Later in the intervals between these 4 prolongations of the embryonic area, 4 more outgrowths take place as a rule in *T. hybrida* and evidently in some instances 4 more are added to the series. Each one of these separated outgrowths then passes through all the stages of individual embryonic development and in the end 8 or 12 identical embryos are developed within a common chorionic cavity. Each has its own umbilical cord and each its own placental area differentiated in a common zonular placenta. Each is in its own amnion but the separate amniotic cavities are all connected with the original common point of origin of all the embryos, by a series of small amniotic canals.

It would seem that in *T. hybrida* the cleavage of the original embryonic plate is

normally into 8 or 12 and that when odd numbers of foetuses are present later on in pregnancy the reduction occurs as a result of overcrowding in the uterus and subsequent abortion of some of the number. There would seem to be some disadvantages in the attempt made by this species of armadillo to produce eight or a dozen foetuses and to accommodate them in a uterus that seems so obviously designed to accommodate only one.

In the same year (1909) as that in which Fernandez described the strange happenings in *T. hybrida*, H. H. Newman and J. T. Patterson published a preliminary report of their investigation into the reproductive history of an allied species (*T. novemcincta*) the Pebas or Nine-banded armadillo of Texas. In this species the processes are exactly the same as in *T. hybrida* save that when the embryonic plate has produced its 4 outgrowths no further subdivisions are formed. The result is that in this species 4 identical same-sexed foetuses are produced at every pregnancy. Newman and Patterson were careful at the outset of their enquiries into the stages of embryological development to determine the fact that "there is never more than one true corpus luteum in the ovaries of a pregnant female." In *T. novemcincta* as in *T. hybrida* the ideal number of same-sexed identical foetuses is not invariably present. In Newman's series of over 200 pregnant uteri there were two in which only 3 were present and in one of these there were obvious traces of the aborted fourth member. In three cases five foetuses were present and in one of these the remains of a degenerating sixth embryonic rudiment were present.

Perhaps few facts in systematic zoology are more puzzling than that demonstrated in the profound anatomical and physiological differences between two such obviously nearly allied animals as the spotted

hyena (*Hyaena (Crocuta) crocuta*) and the striped hyena (*Hyaena striata*). The spotted hyena, as we have seen, contradicts every rule of ordinary mammalian sexual development, while the striped hyena is perfectly normal in this regard.

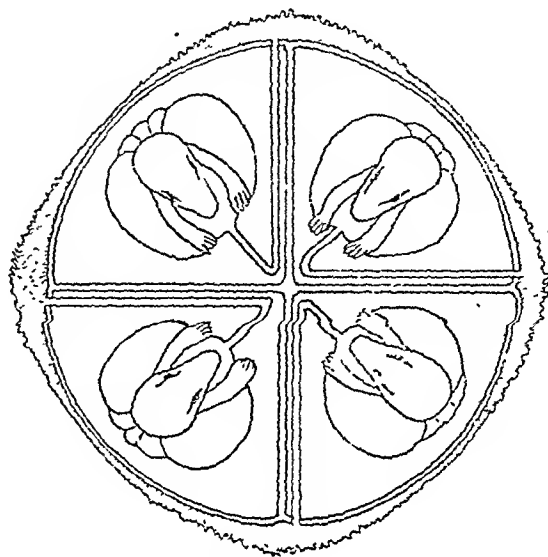


FIG. 25.

The four uniovular foetuses of *Tatusia novemcincta* to show their symmetrical arrangement in the uterus. (After Newman.)

The Mulita armadillo and the Nine-banded armadillo are so nearly allied as to have been regarded by some mammalogists as merely local varieties of the same species.

It is surely a remarkable thing that these two creatures should have resorted to this strange method of producing multiple offspring from a single ovum and still more strange that while the one species produces 4 in a litter, the other has elected 8 or 12.

The genus *Tatusia* is not the only assemblage of South American armadillos, for other forms, distinguished by certain characters that will be discussed later, are embraced in nearly allied genera. Of these, the members of the typical genus *Dasybus* are of outstanding interest. The reproductive

history of the 2 species, the Six-banded armadillo (*D. sexcinctus*) and the One-banded armadillo (*D. gymnarus*—*Xenurus unicinctus*) has been studied with more or less completeness. Von Kolliker and Chapman are agreed that these species normally produce only a single offspring at a birth, but the birth of two young has been recorded in the case of *D. sexcinctus* in the Philadelphia Zoological Gardens. But the most disconcerting of all the members of this genus is the Hairy armadillo or Peludo, *D. villosus*. In 1915, Fernandez announced the curious finding that in this species 2 foetuses commonly occupy the uterus and these foetuses seem to present every evidence of being derived from a single ovum. The 2 foetuses appear to be contained in a single chorion, separated from each other by what at first sight seems to be their fused amniotic membranes. Each foetus has its own umbilical cord and share of a zonular placental area. But the strange discovery that Fernandez made was that in the first 10 pregnancies he examined, the 2 embryos were both males in one case, both females in 2 cases and in seven cases they were of opposite sex. Although the embryos appear to be enclosed in one chorion and although the general appearance of the pregnancy resembles so much that typical of the members of the genus *Tatusia*, the fact that the pairs of embryos are not invariably of the same sex seemed to prohibit their origin from a single ovum. Fernandez examined in all 34 uteri containing embryos in every stage from primitive streak formation to full term. He found that the 2 embryos quite definitely started from 2 separate ova and that these 2 embryos crowded together in the simple uterus had become so closely approximated during development that their membranes had fused together and become thinned out over the area of fusion to such an extent as to produce the appearance of a single

chorionic vesicle containing two embryos separated only by their amnion. Two further interesting facts were revealed by Fernandez during this investigation, for he found 5 cases out of his 34 pregnancies in which only one embryo was present in the uterus. He also noticed that in young females that had never been pregnant the uterus still showed evidence of bicornuate structure.

What sort of generalization can possibly be deduced from this strange assemblage of facts? Obviously any suggestion of generalization can be but little better than guesswork. But there are one or two deductions that may be drawn with comparative safety from the anatomical findings.

In the first place it seems justifiable to assume that all members of the *Bradypodidae*, *Myrmecophagidae* and *Dasypodidae* alike have in their phylogenetic story gone through the phases of structural adaptation of uterus, ovaries and mammary glands typical of mammals that produce only one offspring at a pregnancy. It is only of the *Dasypodidae* that we know sufficient facts concerning reproduction to obtain any insight as to the changes that have happened or to make even the most tentative guess as to the causes of their happening. Of the family *Dasypodidae* it is only of the two genera *Tatusia* and *Dasypus* that we have sufficient data to make dogmatic statements. So far as the different species of these two genera that have been examined can tell us it seems true to say that members of the genus *Tatusia* produce multiple, same-sexed uniovular embryos, while those of the genus *Dasypus* produce either single embryos or two that, in the case of the only species so far fully studied, are, or may be, opposite sexed, and are derived each from a separate ovum despite their deceptive monochorial appearance. Anatomically, the differences between members of the two genera *Tatusia* and

Dasypus, as these genera are generally defined, may be summarized as follows:

TATUSIA.

There are milk precursors of the permanent teeth.

There are only 4 digits on the manus and 5 on the pes.

A pair of inguinal mammary glands is present in company with a pair of pectoral glands.

The uterus does not show any sign of the primitive cornua.

DASYPUS.

There are no remains of a milk dentition.

There are 5 digits on both manus and pes.

Only a pair of pectoral mammary glands is present.

Presence of uterine cornua indicated in uterus of young female.

It may be correct to state that of the armadillos, *Tatusia* "is the most aberrant form" (Flower and Lydekker, 1891), but it retains at least one primitive feature in the possession of a partial milk dentition and probably another in having 4 instead of 2 mammary glands. Both genera are geologically ancient and all their known ancestors are confined to South America where remains of members of the existing genera are present in pleistocene deposits. Unfortunately, no definite conclusions as to the habits of their more remote ancestors in the Miocene of Santa Cruz in Patagonia or in the earlier Eocene beds can be safely drawn from their fragmentary remains. We can therefore only guess at the factor that caused them, at some remote period in their story, to bring about all the anatomical changes that are typical of a single-birth pregnancy. Perhaps the most likely guess is that, since all the members of the *Myrmecophagidae*, save one, are arboreal and all the *Bradypodidae* are rigidly confined to a life in the tree-tops, it was the arboreal habit that was the determining cause. Although it might seem that armour-plating is incompatible with abor-

real life it must not be forgotten that it is possible that this was more highly developed subsequent to the descent from the trees and with the adoption of terrestrial life. And it must not be overlooked that among the armoured Edentates of the Old World (*Manidae*) many of the Pangolins or Scaly anteaters are true tree-climbers although a few of them have abandoned arboreal habits and have become terrestrial and burrowing animals. The existing armadillos are terrestrial creatures and all accounts of their habits are agreed upon the expertness of their methods of burrowing and upon the depth of the retreats in which they have their homes and produce their young. I know of no account of their life histories that suggest any possible remaining aptitude for climbing but that is not surprising in a group of animals so little studied in intimacy.

Whatever it may have been in habit and environment that dictated all the anatomical changes of uterus, mammary glands and ovaries towards the end of begetting a single offspring at a birth, it is very evident that the present circumstances of habit and environment make no such demand. Beyond all animals, the one that has a nursery safe in the depths of a burrow can afford to produce large litters. It might be hazarded that the members of the subfamily *Tatusiinae* had, at an earlier phylogenetic stage, so specialized in uniovular ovulation that when change of circumstances had resulted in the possibilities of dealing with larger litters the only method of producing them was by the subdivision of the single ovum. The difficulty of the single pregnancy uterus was overcome by the extraordinary mechanical and symmetrical arrangement of the resulting embryos in the uterus. But I know of no observation concerning the method of suckling of the numerous young at the limited number of nipples. That the dis-

parity between the number of functional mammary glands and the number of offspring produced at a birth is no insuperable obstacle to the successful rearing of a family we know from the case of the guinea-pig. In this animal there is but a single pair of mammary glands, but the number of young in the litter may considerably exceed this. In this connexion it is worth noting that both the guinea-pig and the *Tatusias* have exceptionally long gestation periods. The guinea-pig is pregnant for nine weeks, the Peba armadillo for twice that period and the milk requirements of young animals born mature and after prolonged periods of gestation are well known to be less than those of more immature offspring.

Of the members of the sub-family *Dasypodinae* it might be hazarded that they are still capable of producing more than one ovum at the period of ovulation and that frequently 2 at least are shed and fertilized. The only difficulty to be faced is the implantation of 2 pregnancies in the simple uterus adapted for the accommodation of only a single foetus. Here resort is made to the same sort of symmetrical packing as is adopted in the case of the *Tatusias* with the result that diovular foetuses appear to be monochorial.

Two speculations suggest themselves from a study of the reproduction of the armadillos. The first is that caution must be exercised before apparently monochorial foetuses are diagnosed as being necessarily uniovular in origin. And the second is that the production of uniovular twins might be expected to be confined to those animals that have carried out all the readjustments of uterus, mammary glands and ovaries associated with the habitual begetting of a single offspring.

HUMAN AND OTHER TWINS.

There would seem to be but little temptation to produce more than one offspring

from a single ovum in cases in which many ova are shed in a single act of ovulation. Indeed we know that in the mammals that produce large numbers of offspring at each pregnancy there is often, if not invariably, a shedding of ova in excess of the number of young that are actually born. There are ova enough and to spare to provide for these multiple pregnancies for not all the ova that are fertilized ever reach maturity. Some are aborted in early stages of development by overcrowding in the uterus. Some perish by lack of a sufficient blood supply. Some are too late in their arrival in the uterus. Even when all the embryos are successful in arriving at maturity and all of them have succeeded in being born they may still be in excess of the number that are destined to grow up. It is well known that some of the marsupials produce more embryos than they have nipples in the pouch and since the immediate grasping and retention of a nipple is essential to life some of these excess embryos inevitably perish. As a general rule therefore we may say that multiovular mammals tend to produce ova in excess of the young normally reared as the result of a pregnancy. There is no need to subdivide a single ovum in order to provide a litter.

But if any group of mammals has established the physiological rhythm of producing only one mature ovum during each period of ovulation its only possibility of producing multiple embryos is to subdivide the single egg. This is what the armadillos of the genus *Tatusia* have to do and, as we have seen, *T. hybrida* makes one ovum go so far as to produce as many as a dozen embryos and *T. novemcincta* makes 4 as its normal litter.

It would be a matter of the greatest interest to know how widespread this business of producing more than one embryo from a single ovum may be in the mammals. Unfortunately the known facts are

so few that it is only possible to speculate on the subject. In the first place, before dogmatic statements could be made, it would be necessary to know precisely how many definite corpora lutea there were in the ovaries of the mother. In addition, the early stages of embryonic development would have to be definitely known and lastly the general likeness and identity in sex of resulting embryos would have to be ascertained. We do not know all these things concerning any of the mammals that might be considered likely to produce uniovular young.

It is, of course, only among the mammals that have gone some way towards the development of a single pregnancy type of uterus and a reduced series of mammary glands that we would be likely to find this method of producing multiple offspring. Two interesting classes therefore suggest themselves in this connexion—the volant mammals and the arboreal mammals. In both cases we know enough to make the question a tantalizing one, but one that cannot be solved by the facts so far available.

Concerning the volant mammals we have one very definite fact that is suggestive of further possibilities. Fortunately in his investigation into the reproductive story of the horse-shoe bat, Harrison Matthews recorded the fact that "*only one (corpus luteum) is present in each female, in the right ovary and no corpora lutea atretica were found accompanying it.*" It is strange that all investigations into the anatomy of the Cheiroptera are agreed that only the right ovary has ever been found to contain a corpus luteum and only the right uterine cornu has ever been seen to contain the embryo. This would seem to be the most extreme case of the limitation of ovulation—that one ovary should be selected to produce the single ovum shed during ovulation. In the armadillos, although only 1

corpus luteum exists it may be found in either ovary, for both seem to be equally functional. The bats are not unique among the mammals in specializing in the functional activity of only one ovary. So far as is known, all the Monotremes, though possessing 2 ovaries and oviducts produce ova only from the left ovary. In these animals the selection is of the left sex gland, as is the case among birds, whereas in the bats it is the gland of the right side that alone functions.

Concerning the bats we also know that only a single embryo is ever produced by any species in Great Britain. But some species (such as the *Pipistrell*) which here produce a single offspring commonly have 2 in continental Europe. And here, just where the question becomes most interesting, our knowledge of facts ceases. So far as can be ascertained there is no record of the sex of the two offspring nor of the number of corpora lutea present in the ovaries of the mother. It is impossible to guess if the two young produced by the bats in France and Germany are uniovular or multiovular in origin.

Concerning the arboreal mammals there is the added interest that Man must be included in their number. Much light could be thrown upon this subject by a careful investigation into the reproduction of those monkeys that readily breed in captivity, for most monkeys occasionally produce 2 young at a birth. Facts as to the similarity or dissimilarity and the identity or difference in sex of the two young are necessary and, above all, the number of the corpora lutea, before any further advance can be made towards shedding light on the problem as it is presented by the lower Primates.

In the case of Man it must be admitted that our ignorance is almost complete and most of the accounts of the origin of human twins and multiple pregnancies are little

better than guesswork decked out in scientific trappings. In 1917 Newman wrote: "The evidence furnished by the *data* collected by obstetricians of twins *in utero* also favours the existence of monozygotic twins. Frequently this evidence is lacking in very essential points. Sometimes, for example, the sex is not mentioned, and never, so far as I am aware, is there information about the number of corpora lutea present. The importance of the latter *data* cannot be overemphasized in this connexion; a knowledge of whether one or more corpora lutea are present would furnish a crucial test of the number of ova concerned in a given pregnancy. *In not a single case of human multiple births, so far as I am aware, has the number of corpora lutea been noted.*" Failing this knowledge Newman pins his faith upon more scientific accounts of the conditions of placentation and disposition of the foetal membranes and he says: "Although *data* as to intra-uterine relations are incomplete and inconclusive, they form the only really direct evidence now available on the mode of twinning in Man." But even this evidence has to be treated with the greatest caution however scientifically it is recorded. In the case of *Dasypus villosus* we have seen how diovtular embryos may by early readjustments of their foetal membranes in the confined space of a single-pregnancy uterus present every appearance of being monochorial twins.

What would seem to be most probable is that Homo, having produced a typical single-pregnancy type of uterus and a reduced series of mammary glands during the phylogenetic past, can in present circumstances of habit and environment face multiple pregnancies despite the initial anatomical handicap. Multiple pregnancies in Man may result from a reversion to the more primitive mammalian method of shedding several ova at an act of ovulation

or it may be brought about by the armadillo's method of making more than one embryo from a single ovum. It is best to say that we have not sufficient evidence to determine which is the method most commonly employed. It seems safe to say that opposite-sexed pairs are certainly diovtular in origin and that same-sexed pairs may or may not be uniovtular. Even among the 4 uniovtular foetuses of *Tatusia novemcincta* there is not absolute identity in all characters but there is a very definite and striking similarity between them. A very striking similarity between the 2 members of a same-sexed pair of human beings is strong presumptive evidence of their uniovtular origin. Perhaps that is as far as it is safe to go and possibly it would be a gain to limit the term twins to human paired, same-sexed offspring that exhibit a high degree of general similarity.

The reason why it might be desirable to limit the term twins to what are commonly termed "identical twins" is that confusion with what are termed twins among lower animals would be avoided. When an animal which normally produces fairly large litters, produces only 2 young we do not commonly apply the term twins to them. We do not speak of twin rabbits if the mother chances to produce only two. But with such domestic animals as generally produce only one at a birth the occasional 2 that are begot are commonly termed twins. The use of this term opens up the old questions of twinning in Ungulates and the production of the freemartin.

John Hunter (1786), Numan, the Dutch veterinarian (1843), Spiegelberg in Germany (1861), Berry Hart (1910), L. J. Cole (1916) and F. R. Lillie (1916) are among the prominent workers who have helped to build up a vast literature on the subject of the freemartin. But the freemartin does not, as has been so commonly held, provide any evidence in favour of the

uniovular origin of ruminant twins. Lillie has shown quite conclusively that the free-martin is a female, aborted in the development of its proper female sexual characters, by the male hormone passing into its circulation, which has become confluent with that of the fully sexed bull with which it shares the uterus. It is impossible not to agree with the summing up of Lillie's work by Newman: "The work leaves no question as to the dizygotic origin, not only of opposite sexed, but also of same sexed bovine twins. Whether real monozygotic twinning ever occurs among the Ungulates is highly questionable."

So far as is at present definitely known the production of more than one embryo from a single ovum—or what might perhaps be properly termed twinning—occurs only in Man and the Armadillos of the genus *Tatusia*. It might be expected to occur at times in other Primates and in the Bats, but we should not look for it outside the limits of those animals that, having in the phylogenetic past reduced the uterus, the ovary and the mammary glands to the single-pregnancy type, find it possible, perhaps by changed circumstances, to be pregnant of and to rear more than one offspring at a birth.

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Full-time Intraligamentous Ectopic Gestation

BY

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THE intraligamentous type of tubal gestation is sufficiently rare to warrant the recording of details of every case. This becomes increasingly so in those few instances which succeed, despite the abnormal location of the gestation sac, in proceeding to term.

The case in question is that of a full-time anterior subperitoneal intraligamentous pregnancy which was discovered in one of the bodies sent to the dissecting room of this Department. The previous history, as obtained from departmental records, showed that the patient was a Sinhalese, 29 years old. This was her second pregnancy; the first resulting in a normal delivery 8 years ago.

I. PRELIMINARY EXAMINATION OF THE CADAVER.

The body was that of a very well nourished woman of average build; weight 100 pounds. On abdominal palpation a hard mass, thought at first to be a foetal head, was felt high up to the left of the middle line, and the foetal back on the right side.

An attempt to withdraw some amniotic fluid (by inserting a needle through the middle line below the umbilicus) for the purpose of injecting formalin, was a failure.

II. NOTES ON DISSECTION.

The body was opened by two paramedian incisions to avoid injury to the linea nigra which, despite the deep pigmentation of the general bodily surface, was very pronounced.

A horizontal incision was then made above the umbilicus and the flaps turned back.

1. The gestation sac.

A large thin-walled sac occupied the centre and right of the pelvis and lower abdomen. The thin wall of the sac was accidentally penetrated by the knife and revealed the back of a full-time child whose buttocks were disposed upwards and to the right and whose head was later discovered well down in the pelvis in the right occipito-anterior position. Amniotic fluid was absent; the membranes lying on the surface of the child. The anterior (peritoneal) wall of the gestation sac was reflected along the inguinal region on the posterior aspect of the anterior abdominal wall. The stretched ligamentum teres extended across the sac towards the internal abdominal ring. The caecum and appendix were closely adherent to the top of the sac on its extreme right. The right Fallopian tube was found along the upper edge of the sac. The right ovary was normal and to the right of the tube, and above the sac.

2. Uterus.

This organ was displaced to the left and upwards and was enlarged to the size of a foetal head and hard to the touch. It was this object which had given the impression of a foetal head on abdominal palpation prior to anatomical exploration.

The following measurements were recorded:

| | | |
|-------------------|---------|------------------------|
| Length | - - - - | 6 inches. |
| Breadth | - - - - | 4 inches. |
| Thickness of wall | - | $1\frac{1}{2}$ inches. |

A window dissection made on the anterior wall of the uterus showed that the head of the child was making its way through the side wall of the uterus at its junction with the cervix and the body of the uterus was pushed up and to the left, 'sitting,' as it were, on the head of the child.

On vaginal examination the cervix was found to be thickened and the os admitted one finger, but it was possible to meet a finger from the other hand placed in the pelvic extension of the gestation chamber, proving that an attempt had been made by nature to discharge the child into the natural passages.

Further dissection revealed that the aperture so formed in the right lateral fornix extended upwards affecting the right aspect of the cervical canal and also the right lateral wall of the lower uterine segment, but these deficiencies were closed by the placenta, which had gained attachment to the lateral uterine wall.

3. Fallopian tubes.

The left tube was normal in length ($3\frac{1}{2}$ inches), but was compressed, with the left ovary against the side wall of the pelvis by the enlarged and displaced uterus. The right tube was stretched to $4\frac{1}{2}$ inches. Its ampullary portion was thickened and swollen, the swollen part measuring 2

inches by $1\frac{1}{4}$ inches and opening below into the gestation sac, thus suggesting that this part of the tube was the primary location of the ovum.

4. Placenta.

After opening the gestation sac and withdrawing the foetus, the placenta was found attached to the medial half of the upper part of the anterior wall of the sac; passing thence on to the right lateral wall of the body of the uterus, between the two layers of the broad ligament. Its upper margin gained the Fallopian tube, but whether or not there was any original placental attachment, or alternatively, whether this was due to secondary extension, cannot be definitely stated. The area in contact with the uterine wall included the portion of the latter that had been eroded, producing the rupture already referred to in dealing with the uterus.

5. Child.

The child was a well developed, full time male of 18 inches crown-rump length, weighing 3 pounds $1\frac{1}{2}$ ounces. The umbilical cord measured $19\frac{1}{2}$ inches long.

DISCUSSION.

All obstetrical authorities agree on the rarity of the secondary intra-ligamentous or mesometrial type of ectopic pregnancy. Eden and Lockyer¹ maintain that many, if not most, of the examples in the literature are not true intra-ligamentous pregnancies, but are subject to explanations other than that needed to produce the mesometrial location of the gestation sac, i.e. the rupture of the lower wall of a tubal gestation sac, whereby the foetal membranes are enabled to expand by separation of the two layers of peritoneum comprising the broad ligament, without rupturing them and becoming intraperitoneal. These authors



Photograph of pelvis with intra-ligamentous pregnancy at term. The abdominal wall has been opened and the child removed and placed to the right of the pelvis. The umbilical cord is seen proceeding towards the placenta which is still in situ. The uterus is seen to the left of the median line.

that women who are potential hypertensives develop hypertension at an earlier period in pregnancy than others do, and the hypertension is therefore of longer duration. It is evident that there is no justification for the premature termination of pregnancy with the purpose of making the mother less liable to permanent hypertension. Pregnancy may still be interrupted if there seems to be a risk of eclampsia or after the foetus is viable, i.e. at the end of the 37th week, if this is considered necessary, owing to the severity of the toxæmia, to save the foetus from death *in utero*.

Does pregnancy aggravate hypertension already existing when pregnancy starts? If the conclusions of this paper are correct it is evident that it does not. Not only is there no increased incidence of hypertension in parous women compared with nulliparae, but there is no significant difference between the mean blood-pressures of the two groups at any age. A patient who has chronic hypertension of severe degree at the onset of pregnancy runs a considerable risk of losing her baby, but there is no evidence in our series that pregnancy has any deleterious effect on the remote prognosis for the mother.

SUMMARY AND CONCLUSIONS.

1. An analysis has been made of the blood-pressures of 1,956 women. Of these, 915 were nulliparous and 1,041 parous.
2. Statistically significant differences could not be found between the mean level of blood-pressure in nulliparous and parous women at any age.
3. There was no statistically significant difference in any age group between the percentages of nulliparous and parous women with blood-pressures over 120/80 over 140/90.
4. The number of pregnancies had no demonstrable effect on the mean level of blood-pressure in parous women.

5. Pregnancy does not cause chronic hypertension. The level of blood-pressure in parous women is the same as it would be if they had never been pregnant.

6. Pregnancy does not aggravate a tendency to hypertension, neither does chronic hypertension develop earlier in parous women.

7. Though hypertension is a common remote sequel of toxæmia of pregnancy it is not caused by the toxæmia. Patients who develop hypertension following a toxæmic pregnancy would have done so if they had never been pregnant. A tendency to hypertension often contributes to the severity of toxæmia.

8. Toxæmia of pregnancy may be regarded as a temporary disorder closely associated with pregnancy and leaving of itself no permanent lesion.

9. There is therefore no justification for terminating a toxæmic pregnancy prematurely in order to protect the mother from chronic hypertension.

10. There is no evidence that pregnancy permanently aggravates hypertension already existing when pregnancy starts. There is therefore no justification for terminating an early pregnancy in a patient who has essential hypertension.

Our thanks are due to Mr. W. J. Martin of the Department of Epidemiology and Vital Statistics, University of London, for his invaluable help with the statistical work embodied in this paper.

The Frequency Distribution Curves of blood-pressure relative to Tables I and IV will be found at the end of this paper (Figs. 1 to 8). In each case the ordinate represents the number of patients whose blood-pressure falls within the 10 mm. groups in the abscissa. For reasons of space a single number only is given in the abscissa in each case; for example, "120" represents the group whose blood-pressure falls between 120 and 130 mm. of mercury.

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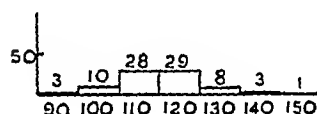
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FREQUENCY DISTRIBUTION OF BLOOD PRESSURE

AGE GROUP 10-19

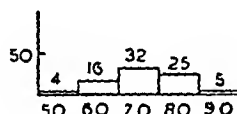
Nulliparae 10-19 Systolic B.P.

TOTAL 82 MEAN 119.4 mmHg SD 11.0



Nulliparae 10-19 Diastolic B.P.

TOTAL 82 MEAN 76.3 mmHg SD 9.6



Multiparae 10-19 Systolic B.P.

TOTAL 3 MEAN 109.0 mmHg SD 49.6

Multiparae 10-19 Diastolic B.P.

TOTAL 3 MEAN 69.0 mmHg S.D. 4.9

Figure.1.

maintain that the rupture of blood vessels in this event would lead to haemorrhage sufficient to cause the death of the foetus; therefore examples which proceed to term cannot be regarded as due to this kind of tubal rupture. Jellet and Madill² on the other hand, aver that the support given by the layers of the broad ligament is such that any accompanying haemorrhage is limited. In any case, what usually happens apparently, is that the gestation sac, whichever way it comes to lie in the broad ligament, succumbs to the accident and a haematocele is the consequence. Nevertheless, it is generally admitted that individual instances can withstand the process and do occasionally carry on by virtue of the activities of the foetal membranes, whereby the placenta affixes itself to neighbouring tissues and draws therefrom sufficient nutriment for the foetus to survive till term. Many, however, undergo secondary rupture due either to stretching from foetal growth or to the erosive powers of the placenta. Such rupture may be into the general peritoneal cavity or into the genital passages; or occasionally both. These cases are attended by fatal consequences to the woman.

It remains to state why the present example is claimed as a true intra-ligamentous gestation, secondary to tubal pregnancy. This may be best accomplished by ruling out the other possibilities which are: (i) interstitial (tubo-uterine) pregnancy, (ii) ordinary tubal gestation, (iii) pseudo-ligamentous gestation. The first alternative seems to be the most likely and the secondary rupture into the right side of the uterus is somewhat in its favour. But against this explanation we have the fact that the gestation sac is not covered anywhere by muscle, nor does it show any evidence of the remains of uterine tissue over its surface, while the site of the rupture is too low down for a pregnancy commencing in the intra-

mural portion of the tube. Moreover the anatomical appearances and the site of placental attachment suggest almost incontrovertibly that the rupture has been due to erosion from without. Also the relations of the sac at term would necessitate the assumption that a double rupture, inwards and outwards, had occurred if the sac commenced its growth at the tubo-uterine junction—and, though such cases of double rupture are known, they are very rare.

It might be possible to explain some cases of apparent mesometrial location of a gestation sac to the continuance of an ordinary tubal gestation which had ruptured intraperitoneally and become secondarily covered with serous membrane derived from inflammatory tissues. This explanation is not very convincing, but might cover some examples where the peritoneum had not been stripped off the anterior abdominal and pelvic walls or the posterior wall of the cavity. As the stripping had occurred chiefly anteriorly in the present case, though not to such a degree as in Berry Hart's³ example, it is not considered that the explanation just given is adequate. Added to this is the fact that the peritoneum is comparatively undisturbed posteriorly, so that the gestation sac has a complete peritoneal covering, except where it is connected with the tube and lateral uterine wall. Moreover the dislocation of the uterus to the left is too great to be accounted for except by virtue of a true mesometrial site for the sac.

The pseudo-ligamentous gestation is rather a special variety of the preceding. It commences in the ampullary portion of the tube, which, instead of rupturing, becomes inordinately stretched over the growing sac contained within. As it stretches, the tubal wall becomes secondarily attached to the posterior layer of the broad ligament and so the sac appears to be contained within the latter. The prob-

able commencement of the pregnancy in the ampullary portion of the tube in the present instance is evidence in favour of this interpretation, especially when it is considered that true mesometrial pregnancy most usually starts in the isthmic region of the tube. But the ventral growth being the principal feature in the present case, argues against the diagnosis of pseudo-ligamentous pregnancy.

So we are left with the conclusion that we are dealing here with a true mesometrial pregnancy. The pregnancy has proceeded to term and the erosive action of the placenta has produced a secondary opening into the birth canal. Lack of expulsive power around the wall of the gestation sac

has resulted in the foetal head becoming impacted in the maternal pelvis; and the mother has died, not from haemorrhage so much as shock, although some haemorrhage from the lower part of the placenta was probably a precursor of this.

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REVIEWS OF HOSPITAL REPORTS

REPORT OF THE ROTUNDA HOSPITAL.

By the Master, Dr. Ninian McL. Falkiner, and the Staff of the hospital covers the year November 1st, 1942, to October 31st, 1943. Before passing to the substance of the report a fitting tribute is paid to the memory of the late Sir William de Courcy Wheeler, who had been consultant surgeon to the hospital for many years. The work reviewed has been carried out in the out-patient department, the district, the obstetric wards, paediatric department, gynaecological wards and Social service department.

At the out-patient department there were 38,223 attendances. Of these 15,313 were antenatal visits. Eighty-six per cent of the patients delivered in the hospital attended the antenatal clinic. Routine blood Wassermann reaction is once again advocated on all pregnant women. While the work done in the antenatal department gives great satisfaction, no efficient postnatal clinic has as yet been organized. It is thought that if this could be rectified by establishing a clinic to which both mother and baby could be referred on discharge from the hospital, more patients could be persuaded to continue with breast feeding. Breast feeding has been all too easily abandoned by patients in spite of a campaign in its favour.

The problem of under nourishment has been helped by the establishment of antenatal and postnatal dining centres in various parts of the city. Some 443 patients received meals during the year from these, but on the other hand there were 5,420 deliveries in the hospital and its district. The 8th day of the puerperium is the customary day for discharge from the hospital. By this time breast feeding is rarely properly established and, as is so common, when the first difficulties are encountered the mother gives up the struggle and puts the baby on the bottle. The mother should really have another week in hospital. This problem is by no means confined to the Rotunda where the intern maternity turnover is steadily increasing year by year, reaching 3,884 deliveries in the year under review, from 2,773 in 1934. Longer stay in hospital is therefore impossible. Already overcrowding is serious, as

reflected in the paediatric section. As with the child, so with the mother, overcrowding means infection. The Master's solution is that more women must be confined in their own homes, and the Rotunda would work for that end. As an immediate solution it may work. More and more, however, institutional confinement is being demanded by the populace, and not without reason. It is so much more convenient for many. As long-term policy surely sufficient accommodation should be provided for institutional deliveries, with adequate lying-in beds. This would allow the mother to have a proper rest, often sorely needed. It would then be possible for many feeding difficulties to be overcome while the patient was still under supervision.

In spite of the difficulties under which the hospital is working the report indicates a very high standard of achievement. Of 1,536 district deliveries, and 3,884 deliveries in hospital there were 11 deaths. (1 district, 10 hospital, giving a mortality rate of 0.257 per cent in the hospital, and for the combined service, 0.202 per cent. One death was considered due to haemorrhagic encephalitis following N.A.B. therapy. The patient was admitted unconscious 48 hours after the second injection (0.6 gm.—incidentally erroneously stated as 6 gm. on p 118). She died 7 hours later. Reference is made to 4 other patients whose lives were imperilled. Dr. Falkiner has abandoned the use of arsenicals in the treatment of syphilis in pregnant women and is at present using bismuth. The remaining hospital deaths are critically reviewed and there is nothing to add. The district fatal case was somewhat unusual and considered to be primarily due to malnutrition.

In breech delivery the test of skill is the delivery of the full-time child in the primigravida where there is no other obstetric abnormality. To arrive at this figure was not easy, but the overall foetal mortality is not high.

The induction of labour table shows an unusual feature—surgical induction was performed for 21 cases of dead foetus, while only in 3 cases of dead foetus was drug induction used. Induction of labour was not carried out in any case of sus-

pect disproportion in a primigravida it is stated. Of 10 2nd gravidae, however, 3 had had the first labour induced at 39 weeks; 1 in the first pregnancy had been going to have a Caesarean section, but the foetus died *in utero*, and a 4-pound child was born as a result of a drug induction. In 4 cases, therefore, in 2nd gravidae, induction was performed when it was not known by trial what the patient could do if given a chance. One remarkable case (B.B.5/5/43) is that of a 19th gravida with a flat pelvis who had had 3 previous lower segment Caesarean sections and was admitted with a transverse lie and ruptured membranes but without pains. Pains were induced by bringing a leg down through a 2-finger cervix. She was delivered of a living baby weighing 7 pounds 6 ounces.—“Head difficult by Smellie-Veit.” This case is illustrative of the attitude towards Caesarean section. This operation is avoided so much that one is inclined to think that occasionally zeal outruns judgment. The Caesarean section rate is approximately 1.7 per cent. Of 45 Caesarean sections of which details are given 3 had spinal, 3 general, and 2 local anaesthetics, while in 37 details of anaesthetics are not given.

In the toxæmic section there were 250 cases (6.4 per cent). The incidence of albuminuria is fairly high (181), while the remainder are classified as “eclampsia” (21), “eclampsia” (24), “nephritic toxæmia” (15), and hypertensive toxæmia (11). It would be interesting to know what is the standard of hypertension. In the patient of 46 years with hydatidiform mole and “eclampsia” (A.G. 29/9/43) hysterectomy without opening the uterus would have avoided a number of complications.

In the Paediatric Department there has been trouble. The general paediatric lay-out in the hospital is outlined. Epidemic after epidemic of gastro-enteritis has taken place in the hospital as in Dublin itself. Inadequate nursing, out of date and hopelessly inadequate accommodation for babies are responsible factors. Immediately required are a special isolation department for babies, additional nursing and medical supervision. All told there were 144 neonatal deaths. Twenty-two full-time normal healthy babies died of enteritis. An important observation is that not one of the babies who contracted enteritis and died was wholly or partially breast fed. Such is

the position frankly and critically stated in the report.

The work of the pathological and gynaecological departments is briefly outlined.

The Master and Staff have much of which to be proud. Where results could be criticized adversely they have done so themselves and pointed out the remedy.

CLINICAL REPORT OF THE COOMBE LYING-IN HOSPITAL.

THIS is Dr. Edward A. Keelan's first report as Master of the Coombe Hospital, and covers the period December 17th, 1942, to December 31st, 1943.

The hospital's capacity has been taxed to the full and sometimes overtaxed. More lying-in beds are required. There were 1,877 intern deliveries, and 1,433 district deliveries, making 3,310 deliveries in the hospital service. There were 6,739 attendances at the antenatal clinic.

In intern practice there were 6 deaths among delivered patients, 2 died undelivered of cerebral haemorrhage and 1 died of *B. coli* septicaemia 14 days after transfer (16 days after delivery) to a fever hospital, giving a total of 9 deaths (0.49 per cent). One patient died in the district service. This gives a total maternal mortality of 0.3 per cent in the complete hospital practice. In calculating these mortality rates I have included the 2 deaths in the undelivered patients and also the death of the transferred patient. To exclude them as is done in the opening summary of the report is to exclude 33⅓ per cent of the intern maternal deaths in the service from the calculated mortality rate.

Of these fatal cases there is an instructive case of marginal placenta praevia (308/43). She was admitted at 33 weeks bleeding slightly. Vaginal examination under anaesthesia revealed marginal placenta praevia but treatment was not carried out. Because she lived near by and did not bleed for the next 5 days she was allowed to go home, having been told to report or send for help immediately should bleeding recur. She failed to carry out this advice when bleeding did recur 2 weeks later. Four hours after the onset of bleeding she arrived in the hospital moribund. (Every obstetrician who has treated antepartum haemorrhage expectantly in

hospital must, upon occasion, have cast a longing eye on a much needed bed occupied by an apparently healthy woman who was being kept in hospital merely because she had a slight painless haemorrhage. It is difficult at times to be fully persuaded that such a woman is in imminent danger of death. Yet she is.) One might wonder, if expectant treatment was contemplated, why the examination under anaesthesia on admission? This is not an isolated instance of examination under anaesthesia with detection of placenta praevia and then the adoption of expectant treatment. In case 468/43 the same was done. This practice would seem to invite further bleeding when the evidently desired expectant treatment would have to be abandoned. It has been said that there is a place for the expectant treatment of antepartum haemorrhage, but not for the expectant treatment of placenta praevia.

Turning to the other cases of placenta praevia we find 5 cases of central placenta praevia in which the treatment was "Foot brought down." In none of 19 cases of placenta praevia was Caesarean section performed. There was only 1 maternal death, but out of 17 cases in which the baby weighed 5 pounds or over, there were 7 stillbirths (41 per cent). It is gratifying to note that the Master has stated that his preference is now for lower segment Caesarean section "in those cases of central and marginal placenta praevia, which have been diagnosed under aseptic conditions, and in which the baby weighs approximately 6 pounds or upwards."

Among 9 cases of prolapsed umbilical cord there were 5 living children. Of 4 stillbirths 2 had died *in utero* before admission, 1 was deformed and the mother of the remaining 1 had severe pre-eclampsia. Congratulation is due for successful result to mother and child by lower uterine segment Caesarean section in a primigravida at term (1111/43) with a free disproportionate head, the forceps having been applied outside while the cervix was only one-quarter dilated; there were 5 inches of prolapsed cord in the vagina. What is meant by Case 9 of this table (1504/43) I do not know. "Breech" is stated as the complication of this case of prolapsed cord. The treatment (for the prolapsed cord) is stated as "version." The case does not appear in the table of internal and combined version. Presumably, therefore, the version

was external, and cephalic (the presentation is stated as breech). Yet in the remarks we find "Grav. 7. Aet. 39. Footling presentation. Os full. Extraction."

The mid-forceps rate is 1.5 per cent. When low forceps cases are added, the total forceps rate is 6 per cent. The induction of labour rate is low. There were 6 drug inductions, nearly all for dead foetuses. There were 23 surgical inductions of which 2 were for the prevention of dystocia while the remainder were for a variety of commonly accepted indications and a number of toxæmic cases. The method of surgical induction, however, is usually not stated. Of 23 inductions the method is stated only in 3, and a different name is given in each case for the same method, and by implication a fourth case was induced similarly by puncture of the membranes. How were the remaining 19 induced?

There were 19 cases of new Caesarean section. Disproportion was the main indication in 11, all of which had been in labour for some time. Three of the 19 became morbid on the B.M.A. standard, and in addition 1 died of peritonitis. All 23 repeat Caesarean sections were performed for disproportion. Two of those had each had 6 previous sections, and 1 had had 5 previous sections. All the babies of the new Caesarean sections survived. Among the repeat sections there were 2 neonatal deaths. In one of these there was difficulty in extraction of the foetus on which autopsy showed a small tentorial tear and congestion of the viscera: in the second where the cause of death is not stated, the baby weighed 6 pounds 8 ounces, and the anaesthetic had been open ether.

Accidental haemorrhage occurred in 17 cases. Among these were 1 maternal death, 10 stillbirths, and 1 neonatal death. In general the initial treatment was conservative, treating shock and if necessary, replacing blood loss. Where the cervix was partly dilated and being taken up the membranes were punctured. Repeated small doses of morphine were given for the relief of pain. The table does not state definitely whether the patients were in labour or not when they came under observation. By deduction the majority were in labour. Case 8 (471/43) presumably was not in labour, for the cervix was closed and had to be dilated before the membranes could be punctured. Yet this case does not appear in induction of labour table.

Case 1 (90/43) a primigravida 28 weeks pregnant on admission, is said to be 52 years old. That so unusual an occurrence should pass without comment suggests that the stated age may be a misprint.

The maternal deaths, on the whole, are clearly set out in their own table and some critical comments are made on these in the opening survey (page 3) of the report. The description of case 1659/43 is difficult to follow in the Caesarean section and mortality tables, but when read in conjunction with para (3) on page 3 the picture becomes clear.

The morbidity rate of 2.2 per cent on the B.M.A. standard is very satisfactory.

Extern maternity details are set out on one page by themselves. There was 1 maternal death from uterine infection. Twenty-three children were stillborn (2 macerated) and neonatal deaths were 16.

A list of 387 gynaecological operations performed follows, with details of 3 fatal cases. Notes on the work of the pathological and Almoner's department bring the report to a close.

While certain criticisms have been expressed, this report reveals a high standard of obstetric practice, in which the guiding hand is that of a highly trained conservative obstetrician. The Master is to be congratulated on his first year's work, in which he has upheld the great Irish tradition

MEDICAL AND CLINICAL REPORT

OF THE

ELSIE INGLIS MEMORIAL MATERNITY HOSPITAL, EDINBURGH,

FOR THE YEAR 1943.

THIS report is of a different plan from the two former ones. The survey of the year's work is considered under customary headings. The tables show the total number of cases within each major group with numerical results, which are frequently subdivided also numerically, but in no group are detailed clinical data of single cases recorded. There is, however, a lot of information in this report.

There were 1,310 deliveries (including 25 abortions) in the hospital and 552 deliveries (including 25 abortions) on the district, making a total of 1,862 deliveries (including 50 abortions), in the

complete service. A differentiation is made between "Booked" and "Unbooked" cases. The relation of the former to the latter is roughly 35 to 1.

The maternal mortality in the complete service was 3 deaths—2 in the hospital and 1 in the district practice. Both hospital cases were "Booked." In one death was ascribed to asphyxia from the inhalation of vomit during anaesthesia (gas and oxygen), and in the other to shock following craniotomy for obstructed labour due to deflexed head and compound presentation. The "unbooked" district fatality occurred from valvular disease of the heart. This patient had mitral stenosis with decompensation, and premature (twin) labour set in at 28 weeks. She died 24 days later in a general hospital. Maternal morbidity was 3.7 per cent on the B.M.A. standard, or 2.8 per cent notifiable pyrexia standard. The stillbirth-rate was 38 per 1,000 viable births, and the neonatal mortality 31 per 1,000 live births.

The section dealing with the treatment of antenatal abnormalities is straightforward. It would be helpful to the reader, however, to know what are the standards for the diagnosis of pre-eclampsia. (This applies to all the hypertensive toxæmias in all these reports, because the standards and practice adopted vary so much from hospital to hospital.) Similarly some explanation of the conditions governing the admissions to the department for venereal diseases and vaginal discharge ("L" ward) might have been included. It is stated that 120 adults, and 47 babies suffering from ophthalmia neonatorum, were admitted to "L" ward. Of the 120 adults 20 had syphilis, 9 had gonorrhoea and 91 had non-venereal vaginal discharge requiring in-patient treatment. Some of these figures seemed high for a hospital with 1,310 (including 25 abortions) in-patient deliveries. Inquiry from the hospital reveals that the department for venereal disease is part of the general scheme for the city. Practically all pregnant women, from the city and surrounding regions, requiring treatment are referred to one of two voluntary maternity hospitals of which this is one. This explains the figures for adults. Of the 91 patients with non-venereal vaginal discharge there were in fact 57 admitted for treatment while the remainder (34) were treated as out-patients. As regards the ophthalmia neonatorum figures, these include

"every infant up to the age of 21 days showing any discharge from the eyes however slight." Provision is made for the admission from the district of babies requiring observation. The figure of 47 cases of ophthalmia in hospital cases is a mistake. It should read 34, the rest being district cases. Two of the ophthalmias were gonococcal (1 born in the hospital and 1 outside): neither was severe it seems.

In the breech presentation table the method of arriving at the corrected foetal mortality rate is not clear. Among obstetric operations 3 cases of high forceps (indication prolapsed umbilical cord) are noteworthy. The term high forceps is not often seen now. It is a pity we have not the details of single cases. There were 58 Caesarean sections (13 repeat operations) with, after the exclusion of 2 monsters, a corrected foetal mortality rate of 10 per cent. An unusual indication, for which 4 emergency sections were performed, is the not very explicit term "non-polarity." Induction of labour was carried out on 217 occasions. In 116 cases a combination of medical induction and artificial rupture of membranes was used, medical alone in 87, oestrogen in 6 and balloon induction in 8 cases. Impending disproportion was the indication in 9 cases, but we are not told whether in primigravidae or multiparous patients. It is open to question whether "social and economic reasons, difficulty of transport, conservation of beds, etc." are justifiable indications for 36 combined (medical and artificial rupture of membranes) inductions. There were 59 cases of postpartum haemorrhage or shock. Transfusion of blood or plasma was given on 19 occasions, and the placenta was removed manually in 16 cases.

There is also a bacterial report. It seems that swabs are taken from the fauces and lower part of the vagina in all patients: (a) on admission to the antenatal or labour wards and (b) on the 4th day of the puerperium. Swabs are taken from the cervix before surgical induction is undertaken. The incidence of haemolytic streptococci in the various sites is given. Lancefield grouping is not indicated. We are told, however, that in 14 cases in which the occurrence of haemolytic streptococci was associated with genital infection none was Group A.

In the paediatric section there are many interesting figures. It would be helpful to know

whether specified causes of stillbirth and neonatal death had been confirmed by postmortem examination.

The reading of this report leaves the impression that it is one of possibilities and potentialities. It tells a lot, but prompts many questions. Could it be expanded by single case *data* in its various sections it would be a splendid report.

Detailed clinical reports are most important documents. From them much can be learned, both by those who produce them and by those who study them. When reports from a large number of hospitals over a period of years are collected we have one of the simplest forms of access to large numbers of cases for the study of individual conditions and diseases. Yet they can be disappointing, and their value impaired if the results of one hospital are not comparable with those of another. I should like to plead for more uniformity in the plan of these reports. Surely it ought to be possible to agree on the tables which it is desirable to include in a report. One hospital gives detailed tables of postpartum haemorrhage, manual removal of placenta, trial of labour, primary uterine inertia, etc. and others do not. From those who do not the figures we desire to know may be arrived at by complex searching of other tables and laborious calculation and even then we may be frustrated. There is not agreement on the *data* which should be recorded in the tables which are set out in detail. There is not even agreement on what is meant by terms such as complicated, and uncomplicated breech. Since the last meeting of the Royal Society of Medicine devoted to such Reports a number of years has passed and there have been changes in practice. Hospitals which have cut down their reports to a mere skeleton because of paper shortage and curtailed staff, must be thinking ahead to the time when they can expand them once again.

Should not that day of re-expansion be the time for more uniformity and comparable *data*? Should the Obstetrical division of the Royal Society of Medicine devote another meeting to it or should the Royal College of Obstetricians and Gynaecologists prepare what it considers an ideal form of Annual Clinical Report?

ANTHONY W. PUTTER.

BOOK REVIEW

"The South African Frog (*Xenopus laevis*) in Pregnancy Diagnosis." Weisman and Coates. The sub-title of this book describes it as a research bulletin. In fact, it is mainly a semi-popular account of investigations undertaken largely by Hogben's school between 1930 and 1941 and repeated with some embroidery by the authors between 1942 and 1944.

The book performs a useful service in collecting together most of the published knowledge concerning *Xenopus*, including a comprehensive bibliography and details of the animals' habitat, anatomy and behaviour. It is chiefly concerned with *Xenopus* as a test animal in pregnancy diagnosis though the style adopted results in the inclusion of much irrelevant detail. Instructions are given for maintaining stocks of *Xenopus* and for carrying out the test. One serious fault in their technique is in extraction of the urine prior to testing. The method they recommend was dis-

carded by British workers in 1941 after that published by Scott had been tested and proved. Weisman and Coates, however, condemn Scott's method without trial, claiming 98.9 per cent accuracy in 1,000 cases as against Scott's 100 per cent accuracy in 1,000 cases. An interesting table summarizes the experiences of about 20 groups of workers who have used the animal for pregnancy diagnosis. In the last 10 years nearly 7,000 tests have been recorded with accuracies varying with the worker from 96 per cent to 100 per cent. The authors point out, and give details showing, that the test is accurate, speedy, inexpensive and simple to perform and that the animals are easier to maintain than laboratory rodents. As they summarize: *Xenopus* has "earned its rightful place in the world of science. It should rank on the same and equal plane with the guinea-pig, the rabbit and the rat."

F. W. LANDGREBE.

INDEX TO CURRENT LITERATURE

In this Index an endeavour will be made, so far as war conditions permit, to maintain an up-to-date record of all titles bearing on obstetrics and gynaecology and the infant. The classification aims at making immediately available for the reader the titles under the various subject headings. In the majority of instances the title is obtained from the original publication. Where this has been impossible, the title has been obtained from the abstracting journal shown in brackets. Reprints will be welcomed and should be sent to the Editor.

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Hypoplasia of the Uterus with Special Reference to Spasmodic
Dysmenorrhoea

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DURING the discussion on primary, intrinsic, or spasmodic dysmenorrhoea, at the British Congress of Gynaecologists and Obstetricians, held in Edinburgh in 1923, Eden quoted Mathews Duncan's definition of the condition as "a disease of the nature of neurosis, in which the contractions of the uterus cause great pain." In spite of the many additions to our knowledge since that time, this definition still covers all that is known, with any certainty, about dysmenorrhoea and its causation. None disputes the important part played by the nervous make-up of the individual and, with few exceptions observers are agreed that the pain, which is rhythmical or has periodic exacerbations, coincides with uterine contractions. Indeed a definite association has been demonstrated by studies in which uterine activity has been recorded by means of intra-uterine bags (Lackner and others,¹ Moir²). The character of spontaneous contractions, and the response of the uterus to oxytocic substances, varies according to the phase of the

menstrual cycle. Knaus's³ original suggestion that the greatest activity is shown about the time of ovulation and that the myometrium is refractory during the luteal phase, has not been confirmed, and the clinical experiments of Moir,² Wilson and Kurzrok,⁴ and Bickers⁵ go to show that the quiescent uterus of the post-menstrual phase gradually becomes more active throughout both follicular and luteal phases, reaching a peak just before and during menstruation. They found that during the follicular phase the contractions are frequent but of low amplitude, whereas in the luteal phase the amplitude is high and frequency low. According to Reynolds⁶ the results of these workers are open to question because of possible errors arising from the experimental technique employed, and he, on theoretical grounds, supports the view of Knaus. Nevertheless nearly all are agreed that the most powerful contractions are seen just before and during menstruation; some regard these contractions as the result of a progesterone influence,

this difference cannot be demonstrated by methods which only register the increase in intra-cavity pressure resulting from contractions. The uterus is capable of different patterns of motility; the painless non-expulsive contractions of pregnancy are different from the expulsive and painful contractions of labour. Again the severity of the pain experienced in labour is not proportional to the efficiency of the uterine contractions: sometimes the most distressing pain results when the contractions in labour are incoordinate and the dilatation of the cervix delayed. If during labour, contractions of the uterus, although possibly of equal severity from the point of view of increasing intra-uterine pressure, may nevertheless be different in pattern and in functional efficiency, then we may suppose that such differences may occur in the behaviour of the non-pregnant organ. This brings us to the view that spasmodic dysmenorrhoea is essentially the result of incoordinate muscular activity—a view which is by no means new and is sometimes expressed in terms of a fault in uterine polarity. It is a theory which has much to recommend it and, although there is no experimental evidence to show that the contractions in dysmenorrhoea are incoordinate, yet a disturbance of uterine polarity would fit in with all the known clinical facts concerning spasmodic dysmenorrhoea, whereas other concepts do not. Even the possible rôle played by the corpus luteum would fit in because it has been suggested that oestrogen tends to co-ordinate uterine contractions while progesterone has the opposite effect.

The next question is whether contraction or spasm of the muscle is the direct cause of pain or whether, as suggested by Moir,^{2, 12} it is the ischaemia resulting from powerful muscle action which is responsible. This view, which is attractive, explains dysmenorrhoea on the same basis as

the pain experienced in angina pectoris and intermittent claudication. Even so, it can be stated that, in general, ischaemia of a muscle does not of itself give rise to pain; there must be muscular activity at the same time (Lewis¹³). The possibility of a vascular change being ultimately responsible, in part or whole, for the pain is borne out by what is now known about the part played by vascular spasm in initiating the menstrual flow. And again it may explain observations to the effect that pain resulting from uterine contractions (dysmenorrhoea and "after pains") can be relieved with progesterone without the contractions themselves being affected.

To summarize: the pain in spasmodic dysmenorrhoea is intimately related to contraction of the uterine muscle. The difference between painful and painless contractions is one of type rather than strength. There may be increased muscle tone or tetany but there is much to be said for the theory which supposes incoordinate action or loss of uterine polarity as the basic difference. A corpus luteum effect on the muscle is probably essential to painful contraction but it is not yet known whether the effect is a positive one, or a withdrawal phenomenon. It is possible that muscle activity, and hormones as well, operate to some extent by inducing a state of ischaemia.

Leaving aside the mechanism by which the pain is produced, the underlying cause of spasmodic dysmenorrhoea is the subject for innumerable theories, many of which are contradictory. Theories are based on disorders of the central nervous system, the local nerve connexions, the endocrine control of the uterus, the uterine circulation, and the myometrium itself. These are reviewed by Davis,¹⁴ Cannon,¹⁵ Novak and Reynolds,⁸ Fluhmann,¹⁶ Pullen and Hamblen,¹⁷ Lackner and others,¹ Katz and Parker,¹⁸ Ehrenfest,¹⁹ Witherspoon,²⁰ Kan-

nedy,²¹ and do not require discussion here. Suffice it to say that prominent among the theories put forward is the one which supposes that the abnormal contractions of the myometrium (and it has still to be proved that they are abnormal) are fundamentally the result of an error in uterine development. It is true that occasionally a gross malformation such as bicornuate uterus is the cause of intense pain, but in the vast majority of cases a gross abnormality is not present and in these the uterus is said to be in a state of hypoplasia. Indeed Blair Bell²² stated that even a bicornuate uterus rarely causes dysmenorrhoea unless it is hypoplastic as well. Estimates of the incidence of uterine hypoplasia in primary dysmenorrhoea vary from 20 to 100 per cent (Davis¹⁴) and, although the importance of hypoplasia as a cause of dysmenorrhoea has been questioned by a few writers such as Pullen and Hamblen,¹⁷ Davis,¹⁴ Novak and Reynolds,⁸ Fluhmann,¹⁶ Randall and Odell,²³ the view still enjoys a wide popularity. Four British text-books on gynaecology, picked at random,^{24, 25, 26, 27} give uterine hypoplasia as one of the most, if not the most, important cause of spasmodic dysmenorrhoea. This hypoplasia theory is of long standing and has become almost traditional. It was emphasized by many speakers at the British Congress in 1923, and the discussion at that time reflects opinions which are still widely held to-day. At that meeting Gemmell²⁸ was one of the few to give uterine hypoplasia a relatively unimportant place in the causes of spasmodic dysmenorrhoea, and he rated its incidence at rather less than 10 per cent (34 out of 350 cases).

It is postulated that in spasmodic dysmenorrhoea the uterus may be definitely smaller than normal, although well proportioned, or on the other hand it may be of the infantile or pre-pubescent type, either in size or shape. When the uterus is appar-

ently normal in size and shape then it is said that the hypoplasia is manifested by faulty structure of the myometrium, there being a relatively greater amount of connective tissue as compared with muscle tissue. According to Israel²⁹ and Pullen and Hamblen¹⁷ it was Schultz,³⁰ in 1903, who first emphasized the significance of the relative amounts of muscle and connective tissue. Meaker³¹ says the myometrium of the hypoplastic uterus, like the uterus in infancy, may contain as little as 50 per cent muscular tissue, as compared with 90 per cent in the fully developed adult uterus. This statement by Meaker, although uncorroborated, is widely quoted and indeed it is difficult to challenge since few hypoplastic uteri are removed for section. But it should be pointed out that these figures do not agree with those mentioned by Whitehouse²⁴ who says the proportion of fibrous tissue to muscle tissue in the myometrium is 3:2 in infancy, 2:3 in adult years and 3:2 after the climacteric.

It is well recognized that minor malformations of the uterus, such as acute antelexion of the cervix (cochleate uterus), conical cervix, pin hole os, and congenital retroflexion, are frequently but not necessarily associated with dysmenorrhoea. These too are set down as manifestations of hypoplasia.

If hypoplasia of the muscle causes spasmodic dysmenorrhoea how does it operate? Opinions are many and varied and may be summarized as follows: (a) disproportionate amounts of connective tissue and muscle give rise to irregular or incoordinate contractions, (b) the nerves in the immature connective tissues are under-developed and more sensitive; (c) the uterine cavity is small and results in compression of the engorged endometrium; (d) the under-developed muscle is inelastic; (e) the excessive amounts of connective tissue deprive the myometrium of elasticity; (f)

an associated vascular development defect; (g) the weak muscle allows stagnation of the blood in the pelvic organs, and this in turn leads to pressure stimulation of the nerves with resulting powerful uterine contractions; (h) since the uterine muscle is feeble, greater effort is required to expel menstrual blood.

So far as can be ascertained all these explanations are entirely hypothetical and none has the support of either experimental or clinical observations. In themselves they are not convincing and detailed comment on them seems unnecessary.

The recognition of oestrogens as a means of promoting uterine development, and their ready access in recent years has led to their employment in the treatment of dysmenorrhoea and renewed interest in hypoplasia as a cause of this symptom. Oestrogen therapy for dysmenorrhoea was introduced by Kennedy in 1932, and since then there have been numerous reports on its use^{20, 29, 32, 33, 34, 35, etc.} In 1937, Stacey and Shoemaker³⁵ went so far as to say "the giving of oestrogenic hormones to the patient whose uterus is undeveloped seems to be the only logical indication for the use of hormones in the treatment of dysmenorrhoea." This is an extreme view however, and it would seem fair to say that the attitude of the majority of writers and the practice of most clinicians has been to advise and employ oestrogen when the uterus is considered hypoplastic and progesterone to allay uterine contractions and activity when the uterus is fully developed. For reasons briefly mentioned above the value of progesterone must be open to question on theoretical grounds, but this communication is more concerned with uterine hypoplasia, and its treatment with oestrogens.

It has been our endeavour to collect information as to the importance of hypoplasia as a cause of spasmodic dysmenor-

rhoea, and we hope in discussion to demonstrate the need for a clearer and more rational approach to this aspect of the dysmenorrhoea problem.

In all cases of dysmenorrhoea, particularly spasmodic, it is generally admitted that a nervous factor, low threshold for pain, neurosis or hysteria, plays an important part. Indeed Haman³⁶ has recently reported experimental evidence of a lowered pain threshold in dysmenorrhoea subjects. The patient's attitude to menstruation, her environment, mode of living, general development and posture, the nature of her work and recreation, all have their place in its aetiology, and if they are omitted from consideration here it is not because we wish to minimize their importance but rather to avoid clouding the single issue with which we are concerned.

DEVELOPMENT OF THE UTERUS.

Before presenting the results of our enquiry a brief summary of the present day knowledge of the development of the uterus is relevant. This is based for the most part on the writings of Scammon^{37, 38} and Reynolds.³

The development of the uterus in the foetus in its early weeks is governed by a mechanism similar to that of other tissues. It is determined primarily by genetic characters and brought about by inductors or organizers. It is later under the influence of the gonads and probably other endocrine glands such as the adrenal. Fusion of the Müllerian ducts is completed about the end of the 3rd month of intra-uterine life, and thereafter the uterus undergoes a steady growth, its length increasing in proportion to body length, and its weight in proportion to body weight. Up to the 28th week, its length increases at the average rate of rather less than 1 mm. per week. After the 28th week its increase in size is more rapid as a result of oestrogen pro-

duction by the placenta and at birth it measures 35 mm. (about half the adult size). Within 2 weeks after birth its length is reduced by one third (to 23 or 24 mm.) and its weight by one half. This reduction is due to the removal of the placental oestrogenic impulse, and it affects the body of the uterus chiefly, the muscle fibres being reduced in number and size and the vascularity being decreased.

During infancy and childhood very little, if any, uterine growth takes place, and in a 2 weeks old baby the uterus is approximately the same size as it is in an average 10 year old girl. About the age of 10, further development begins and proceeds apace so that by the time of the menarche, or even 1 to 2 years before the first menstrual period (Scammon³⁷), it reaches adult size. In so doing it nearly doubles its length and increases in mass tenfold. This period of uterine growth coincides with other external evidences of puberty. It is directly related to the menarche, and the later the onset of menstruation, the later the onset of this phase of growth: it occurs therefore in different individuals at any time between 10 and 18 years. This prepubertal development is almost entirely the result of an oestrogen stimulus, probably arising from the ovaries. The fact that the uterus does not grow during childhood is not because it will not respond to a stimulus. Unlike the ovary, which is refractory to external stimuli during the early years of childhood and after the menopause (Engle³⁹), both myometrial and endometrial components of the uterus react to oestrogen at any age. This has been demonstrated experimentally in animals, and can be seen clinically when oestrogen deprivation haemorrhage occurs soon after birth, or in the case of precocious puberty due to hypothalamic lesions and granulosa cell tumours of the ovary. The uterus does not grow during infancy and childhood because the stimulus

for growth (oestrogen) is lacking. The effect of oestrogen is to produce hypertrophy of muscle fibres rather than hyperplasia by mitosis. It does, however, increase the number of muscle cells by stimulating metaplasia of connective tissue cells. True hyperplasia, such as occurs in very early pregnancy, is brought about by progesterone (Reynolds⁷).

In the course of its prepubertal development, the uterus undergoes the well-known change in shape whereby the body becomes proportionately longer than the cervix—the reverse of the infantile state of affairs. Although by the menarche the uterus is fully developed in regard to size and shape, there is some evidence to suggest that it is not fully equipped for the function of childbearing. Thus in both animals and human beings it has been shown that, for some time after the ovarian cycle is fully established, sterility is the rule because the uterus is often incapable of the full response necessary for implantation and development of the ovum. This comes after an interval and it has been postulated that either the uterus does not acquire this capacity until it has been repeatedly subjected to many cycles of ovarian stimuli, or its inherent ability to respond to hormonal agents, although present in infancy, is not fully manifested until a few years after puberty (Reynolds⁷).

It should be noted that this description of uterine development differs somewhat from the one given by Lane Roberts and others,⁴⁰ who quote Halban's work of 1906 to show that the reactivity of the uterus to the ovary only appears towards the end of intrauterine life. Moreover, they say that in rodents prepubertal development occurs in spite of oöphorectomy.

This summary would not be complete without reference to the position of the uterus during development. Novak and Reynolds⁸ say that in foetal and early post-

natal life the uterus is sometimes ante-flexed but not invariably so. Munro Kerr and others²⁷ imply that the corpus uteri is somewhat ante-flexed but that the whole organ is retroposed. It is not easy to find a definite statement with evidence on this point but the common view (Blair Bell,⁴¹ Whitehouse,²⁴ Fairbairn,⁶⁴ Crossen⁶⁵) is that at birth the uterus shows very little flexion or version, its axis being vertical with perhaps a slight inclination forwards. Our impressions gained during the routine postmortem examination of several hundred stillborn babies, confirm this although we have not any records of accurate observations. Ante-flexion (and sometimes retroflexion) only occurs as development proceeds and is not present to any extent until the prepubertal growth phase, or even later. It is certainly present, although perhaps not always in full degree, by the time of the first menstrual period.

We have heard it stated that at the age of 5 or 6 years, the uterus is cochleate in shape and that, as development proceeds, the angulation of the cervix on the body normally becomes less acute. But we cannot trace any published statement to this effect, nor any evidence to substantiate it. It may have arisen from the view which explains acute ante-flexion of the cervix in the adult by supposing a persistence of the infantile position of the cervix (i.e. its axis in line with the vagina) while the corpus attains its normal forward inclination (Crossen and Crossen⁶⁵).

It has been the custom of clinicians in the past to describe underdeveloped uteri as being infantile, prepubescent, or pubescent. From what has been said above, it is clear that the infantile state persists from birth to the prepuberty age. Thereafter the uterus either remains infantile or assumes the adult state and there is little to support the above subdivisions. In theory,

there is perhaps some place for a group in which the uterus is "pubescent" as distinct from "mature"—i.e. when it is fully developed anatomically but is still incapable of full reproductive function, but in practice it would be difficult, if not impossible, to recognize this class.

The conditions necessary for full uterine development are: (1) the uterus must be endowed with an ability to utilize, and to respond to, ovarian hormones, (2) these agents must be produced and be available in sufficient amounts, (3) an efficient circulation to assure an adequate supply of oestrogens to the uterus.

Hypoplasia may result if any of these factors are absent and it is not necessarily the result of defective ovarian function. It not infrequently results because the uterus is incapable of response by reason of some inherent fault. This explains why some patients with no other sign of endocrine disturbance have hypoplastic uteri, and why the administration of oestrogens sometimes has no effect on the size of the uterus or on symptoms such as amenorrhoea. Hypoplasia might also result from the presence of some factor having the power to destroy, or render inactive, the oestrogenic hormone. At present this is largely a hypothetical cause but it has been postulated that disease such as tuberculosis may act in this way (Mack⁴²). It may be added that there is little to support the view, widely held for many years, and recently fostered by Meaker²¹ that, after 20 years of age, the uterus loses its inherent growth capacity. Indeed it would appear that after birth, the uterus possesses little, if any, inherent or intrinsic growth capacity. It has merely the ability to respond by growth to extrinsic stimuli. If it is this responsiveness which is said to be lost, then we shall later put forward evidence to show that such is not the case.

DIAGNOSIS OF HYPOPLASIA.

For the purpose of this study, the records of two series of hospital in-patients have been analysed. These consist of (a) 829 cases of spasmodic dysmenorrhoea, (b) 86 cases of proved uterine hypoplasia. Very early in the investigations it became clear that it is extremely difficult to say when a uterus is hypoplastic and when it is not, and it is probably this fact, together with varied conceptions as the nature of hypoplasia, which accounts in large measure for the oft-repeated statements about the incidence of hypoplasia as a cause of dysmenorrhoea. Opinions are frequently based on the impression of a clinician carrying out bimanual examination, and this often *per rectum* in the unanaesthetized patient. All with experience will agree that an estimate of the size of the uterus gained by such an examination can be very misleading. We have not, therefore, accepted vague statements about the uterus feeling hypoplastic or small as being diagnostic of hypoplasia except when they have been supported by additional evidence.

Symptoms which are often accepted as an indication of hypoplasia are the late onset of the menarche and the occurrence of infrequent or scanty menstruation. Although we shall later raise doubts as to their significance, we have investigated our cases from the standpoint of such symptoms.

The best available method of determining hypoplasia is by mensuration of the uterus and on this we have relied to a large extent. But even this does not give any idea as to the thickness of the uterine wall. Nevertheless, as mentioned previously, the length of the uterus increases progressively with development, and tallies with an increasing weight of the organ, so in ordinary circumstances the length should form a good criterion as to the development of the uterus, as it also does for atrophy.

Meaker^{31, 33} and Meigs⁴⁴ have emphasized the importance of comparing the length of the corpus and the cervix and using the resultant "uterine index" as an indication of development. Such separate measurements are so rarely recorded in our series that we have been unable to make use of the uterine index as means of diagnosis. In any case the value of the uterine index can be disputed because it infers that whenever the cervical canal is unusually long, the uterus is hypoplastic irrespective of the size and development of the corpus. Moreover, our attempts to measure the uterine index in a smaller and separate series have impressed us with the difficulty of recording accurately the separate lengths of cervix and corpus. It is often impossible to detect the internal os with a sound and usually the margin of error in measuring the length of the cervical canal is at least $\frac{1}{4}$ inch—an amount which seriously affects the calculated uterine index.

When using the total length of the uterus as a guide to hypoplasia another difficulty is encountered, that is, to distinguish between hypoplasia and atrophy either of the uterus as a whole, or of the myometrium. In theory the difference lies in the relative length of the cervix and corpus, but at operation it can be difficult and indeed is not infrequently impossible to say whether a uterus has never developed fully or whether full development has been followed at a later date by retrogressive change. When possible we have endeavoured to exclude cases of atrophy but in view of this difficulty it is certain that many are included in the second section of this work. But this is not such a great disadvantage for there is not much difference essentially between the two: development depends on an oestrogen stimulus and atrophy results when such a stimulus is removed. In structure the uterus undergoing atrophy tends to return to its original

state, the relative amounts of fibrous and muscle tissue in the senile and infantile uteri being similar. This confusion between atrophy and hypoplasia is common in the literature but writers do not appear to have been conscious of it or at least do not make comment.

The finding of inactive endometrium might also be indicative of generalized uterine hypoplasia, although this of course supposes that the myometrium and endometrium behave in a similar way in every case. In the majority the development and activity of each probably do run parallel since both have a similar origin and both respond to the same hormonal stimuli. Not all will agree with this assumption, especially the protagonists of the hypoplasia theory of dysmenorrhoea who recognize that in patients with spasmodic dysmenorrhoea, endometrial development and function is usually normal. Meaker²¹ supposes that less oestrogen is required to affect the endometrium than the myometrium but experimental evidence in support is lacking. Indeed Clauberg⁴⁵ says that when oestrogen is administered, a hypoplastic uterus first increases in size and that endometrial proliferation is a later effect. This suggests that the myometrium responds to oestrogen more readily than does the endometrium. Moreover it should be pointed out that in uteri the dimensions of which are small the endometrium is usually thin and inactive, and in those uteri subjected to a prolonged oestrogenic stimulus, as in metropathia haemorrhagica, both endometrium and myometrium undergo hypertrophy. So in arriving at a diagnosis of hypoplasia or atrophy in the second series of cases we have taken into consideration the histological appearance of the endometrium as compared with the time in the menstrual cycle. We also present the details of the endometrial picture in III of the cases of dysmenorrhoea.

Hysterectomy was not carried out on any of the patients in either group so it has not been possible to study the myometrium microscopically and to assess the relative amounts of fibrous and muscle tissue.

CASES OF SPASMODIC DYSMENORRHOEA.

The case records of 829 patients complaining of dysmenorrhoea have been analysed. These cases are selected in so far that only those patients with a typical history of spasmodic pain are included, and all cases in which acquired lesions such as infection, endometriosis and fibroids were either present or suspected, are excluded. Cases of gross uterine malformation such as uterus bicornis are also excluded.

Marital Status and Parity.

Of the 829 patients, 432 were single and 383 married (status unknown in 14); 42 had been pregnant but 15 had had abortions only. One hundred and ninety-five women complained of sterility in addition to dysmenorrhoea: in many of these cases the sterility was the primary complaint, dysmenorrhoea being a secondary consideration.

Age of Puberty.

The history of a late menarche is frequently taken as a possible indication of uterine hypoplasia. It certainly indicates a late onset of cyclical ovarian activity or at least a delay in the ovary reaching its full activities and it is therefore not unreasonable to suppose that it is associated with delayed uterine development. But it does not necessarily mean that the uterus never attains full development—that depends on whether ovarian function, when it is established, is adequate—and in many cases it is, even when menstruation does not begin until the age of 18 to 20 years.

If the figures presented in Table I are compared with those given by Kennedy⁴⁶ who investigated the records of 10,216

women of hospital class in Edinburgh and found the average age of the menarche to be 15.037 ± 0.011 with a standard deviation of 1.707, it will be seen that the age if anything is lower for this series of cases. There is nothing to indicate that the age of menarche in women suffering from spas-

beyond the 16th birthday but all except 2 began to menstruate before the age of 18. If scanty menstruation is to be regarded as evidence of hypoplasia of the uterus, then only about 3 per cent of these cases of dysmenorrhoea suffered from such hypoplasia.

TABLE I.
Age at Onset of Menstruation.

| *Age at last birthday | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | Unknown |
|-----------------------|---|----|----|-----|-----|-----|-----|----|----|----|----|----|----|---------|
| No. of cases | 2 | 5 | 43 | 112 | 160 | 225 | 142 | 77 | 37 | 15 | 3 | 0 | 1 | 7 |

modic dysmenorrhoea is higher than the average. Consequently, and if a late onset of menstruation does imply uterine hypoplasia, there is no evidence that the incidence of hypoplasia in these women is greater than the average, but rather the reverse.

Menstrual Function.

It is often stated that oligomenorrhoea and hypomenorrhoea are symptoms of uterine hypoplasia (e.g. Shaw,²⁶ Hoffman¹⁰). There is some reason to doubt this, but accepting this popular conception at its face value, our cases were investigated to see if they presented a high incidence of these types of menstrual upset. The terms hypomenorrhoea and oligomenorrhoea are used by different writers to mean different conditions and, to avoid confusion, we prefer scanty menstruation and infrequent menstruation.

(1) *Scanty Menstruation.* In assessing the incidence of a scanty flow some arbitrary dividing line had to be adopted and we include here those patients whose cycle was more or less regular within the limits of 24 to 32 days, and in whom the loss lasted 2 days or less. Out of the total of 829, and according to this standard, only 28 had scanty menstruation. Of these, 8 gave a history of the menarche delayed

(2) *Infrequent Menstruation.* The menstrual cycle reflects the ovarian cycle and if a long cycle means impaired ovarian function then it might also mean defective stimulation of the uterus by the ovary and consequent incomplete development. In our series there were only 18 patients whose menstrual cycle was always or usually longer than 32 days, and in several of these the cycles were very irregular. The intervals between menstrual periods varied from 5 weeks to 8 months. Of these 18 patients, 15 began to menstruate before they were 16 and all were menstruating before their 18th birthday. This suggests that infrequent menstruation, except perhaps when the intervals are 3 to 6 months or longer, is not significantly associated with a late menarche. Again, and if infrequent menstruation does signify uterine hypoplasia (secondary to ovarian hypofunction), then the incidence of hypoplasia in this series of women suffering from dysmenorrhoea is low.

Our findings, pointing to a low incidence of scanty and infrequent menstruation among women suffering from dysmenorrhoea, do not support the views of Shroeder¹⁷ and Mazer and Israel.³³ The latter, speaking of primary dysmenorrhoea, say "a history of menstrual irregularities or late appearance of the menarche is

elicited in many instances of this morbidity, suggesting the possibility of a common origin." However, the majority of writers, among whom may be mentioned Taylor,¹⁸ Davis¹¹ and Bickers,⁶ comment that women suffering from dysmenorrhoea do not usually have abnormal menstrual losses, and this majority view is confirmed by our results. Furthermore it should be pointed out that those who support the hypoplasia theory of dysmenorrhoea have always emphasized that adult women with supposedly infantile uteri may, and indeed usually do, exhibit normal menstruation (Blair Bell,²² Clauberg,⁴⁹ Moricard,⁵⁰ Meaker³¹.) Blair Bell and Meaker stress, and rightly we think, that when these types of menstrual disturbance occur in the presence of uterine hypoplasia, they are evidence of an associated ovarian hypoplasia or at least hypofunction. Nevertheless if uterine development is to a large extent dependent on ovarian function, then it is surprising that dysmenorrhoea, if caused by uterine hypoplasia, is rarely associated with disturbance of the menstrual rhythm. This discrepancy can only be explained by assuming that in nearly all cases of dysmenorrhoea due to uterine hypoplasia the fault lies in the inherent failure of the myometrium to respond to the ovarian stimulus, and yet, at the same time, that the endometrium reacts normally. To postulate the occurrence of such a set of circumstances, not as a rarity, but as common, is an explanation of a clinical observation which does not appeal to reason. We prefer the alternative interpretation of the findings, namely, that spasmodic dysmenorrhoea is not often associated with uterine hypoplasia.

Measurement of the Uterus. All our cases were examined under anaesthesia and the uterus measured by sound. The exact measurement is recorded in only 274 cases; in the remainder the operation notes

record that it was normal (i.e. $2\frac{1}{2}$ inches or more). The details are set out in Table II.

TABLE II.

| | | | | |
|--|--------------------------|----|-----|---------|
| 1 | to $1\frac{1}{2}$ inches | .. | ... | 0 cases |
| $1\frac{1}{2}$ | to 2 | .. | . | 3 " |
| 2 | to $2\frac{1}{2}$ | .. | | 12 " |
| $2\frac{1}{2}$ | to 3 | .. | | 106 " |
| 3 | to $3\frac{1}{2}$ | .. | | 108 " |
| $3\frac{1}{2}$ | to 4 | .. | | 45 " |
| " Normal length " ($2\frac{1}{2}$ inches or more) | | | | 555 " |

These figures show conclusively that the over-all length of the uterus in patients suffering from dysmenorrhoea is rarely less than normal. In the whole series there were only 15 cases in which there was definite proof of this. Indeed in a high proportion the uterus was longer than the usually accepted normal. In these cases the uterus was frequently cochleate in type (acute antelexion of the cervix). Other observers have noted that the uterus in dysmenorrhoea is not often reduced in length (Blair Bell²²), and they explain that the uteri are nevertheless hypoplastic because the length of the uterus is made up to a great extent by an unusually long cervix which compensates for the relatively small corpus. In our cases the relative lengths of cervix and corpus are recorded so rarely that we are unable to give statistics but we are of the opinion that when the cervix is abnormally long, then the total length of the uterus is increased, i.e. the body of the uterus remains normal in length and is fully developed.

Although there were only 15 cases in this series in which the uterus was proved to be less than normal in its total length, yet, in conformity with custom, the notes of 120 patients contained a comment that the uterus felt small or hypoplastic on bimanual examination, carried out either with or without general anaesthesia. The actual measurement of the uterus was subsequently recorded in these 120 cases and

in only 9 was the uterus less than $2\frac{1}{2}$ inches in length. In many it was longer than normal (see Table III). These findings go to

TABLE III.

Measurements of those Uteri said to feel small on Bimanual Examination.

| | | | | | | | |
|---|-----|-----|-----|-----|-----|-----|-----|
| 1 to $1\frac{1}{2}$ inches | ... | ... | ... | ... | ... | ... | 0 |
| $1\frac{1}{2}$ to 2 " | ... | ... | ... | ... | ... | ... | 2 |
| 2 to $2\frac{1}{2}$ " | ... | ... | ... | ... | ... | ... | 7 |
| $2\frac{1}{2}$ to 3 " | ... | ... | ... | ... | ... | ... | 28 |
| 3 to $3\frac{1}{2}$ " | ... | ... | ... | ... | ... | ... | 18 |
| $3\frac{1}{2}$ to 4 " | ... | ... | ... | ... | ... | ... | 4 |
| Normal length ($2\frac{1}{2}$ inches and more) | ... | ... | ... | ... | ... | ... | 61 |
| Total | | | | | | | 120 |

substantiate our previous statement that a general impression of size is frequently misleading and should not be accepted as indicating hypoplasia in the absence of other evidence.

Malformations and Malpositions of the Uterus.

Some type of minor developmental abnormality of the uterus was noted in a large percentage of cases, the details being as follows:

Acute ante flexion of the cervix

(Cochleate uterus) ... 368 cases

Congenital retro flexion and retroversion 50 cases

Conical cervix: with or without pinhole os 39 cases

Dysmenorrhoea occurring in the presence of gross malformation such as bicornuate uterus, where the arrangement of the musculature is obviously disturbed, is not difficult to understand but, in regard to the conditions in the above list, the position is more difficult. However it is not unreasonable to suppose that, even in such minor types of maldevelopment, the muscle wave might be affected and the contractions of different parts of the uterus lack co-ordination.

(a) *Acute ante flexion of the Cervix (cochleate uterus).*

This condition, which is common, is widely stated to be a sign of uterine hypoplasia (e.g. Whitehouse,²⁴ Blair Bell,⁴¹ Shaw,³⁶ Wharton,⁵¹ Munro Kerr,²⁷ Meaker,³¹ Mazer and Israel,³³). It always takes a high place in the list of causes of dysmenorrhoea, although estimates of its frequency vary. Gemmell²⁸ put the figure at nearly 20 per cent: in our case it is approximately 44 per cent. The variation is probably explained by the fact that the diagnosis depends entirely on the opinion of individual clinicians. In the hospital from which these cases are taken acute ante flexion of the cervix is a "popular" diagnosis, whereas the diagnosis of conical cervix or pinhole os is rarely made. Although it is recognized that this deformity often exists without the women experiencing painful menstruation, yet it can hardly be disputed that it does appear to play a part. But why should it be regarded as a manifestation of uterine hypoplasia? The evidence in favour is that the cervix is long and narrow, and Blair Bell^{41, 52}, claimed to have demonstrated an excessive amount of fibrous tissue in the region of the internal os. But if the cervix is long and narrow the corpus is usually well developed and certainly within normal limits as regards size. So that the over-all length of the uterus is increased. The menarche in these cases is not delayed, the menstrual flow is full and regular. Although the axis of the cervix more or less coincides with that of the vagina, flexion of the corpus on the cervix, or vice versa, is not characteristic of the foetal or infantile uterus, and it is difficult to understand statements to the effect that both acute ante flexion and retro flexion are "residua of the childhood state" (Mazer and Israel³³). The uterus, as pointed out previously, does not acquire its flexion until its development is far

advanced. Indeed acute antelexion could be regarded with equal reason as a manifestation of over-development as of under-development. According to Schroeder⁴⁷ the extreme angulation of the cervix is due to "contracture" but Crossen and Crossen⁶¹ believe it to be due to a persisting infantile position of the cervix, that is, a failure to develop anteversion, the corpus meanwhile taking up its adult position. Blair Bell⁵² says the localization of fibrous tissue anteriorly at the level of internal os results in the posterior uterine wall growing more rapidly than the anterior, thus making the angle between corpus and cervix more acute. Even if this be so an excessive deposit of fibrous tissue in one special area cannot be taken to imply generalized hypoplasia, neither can a failure of the cervix to become directed backwards. We submit that such evidence as exists does not justify the assumption that a cochleate uterus is an under-developed one, but rather that it is a maldeveloped one. In this connexion we agree entirely with the opinion of Novak and Reynolds,⁸ Davis,¹⁴ and with Gemmell,²⁸ who, as long ago as 1923, questioned the popular view in this respect. Blair Bell^{22, 52} points out that acute antelexion of the cervix is seen in uteri both of normal size and of small size. He, in common with

rather than the size, it is the malformation rather than the degree of development which is the factor causing the dysmenorrhoea.

(b) *Congenital retroflexion and retroversion.*

These types of deformity are again developmental rather than congenital and probably do not appear until development is well advanced. According to Munro Kerr and others,²⁷ retroversion and retro-displacement are common, whereas retroflexion is rare. But opinions—and again it can only be a matter of opinion—must vary, and in many cases the uterus appears to be cochleate in shape and the condition analogous to acute antelexion of cervix. Again there is no reason to regard the malformation as a manifestation of hypoplasia. Although the cervix is long, the body of the uterus is well formed—and menstrual function is good. The cavity of the uterus is usually longer than normal.

Endometrial Patterns.

Not all the patients had curettage performed and full details of both histology of the endometrium and the time of biopsy in relation to menstrual cycle are available in only III cases (Table IV).

TABLE IV.

| Time in menstrual cycle | Proliferative phase | Proliferative phase and hyperplasia | Pregavid phase | Atrophic endometrium | Total |
|-------------------------|---------------------|-------------------------------------|----------------|----------------------|-------|
| 4th to 13th day | 25 | | | 24 | 29 |
| 14th to 20th day | 18 | 2 | 22 | | 42 |
| 21st to 28th day | | 2(a) | 34 | | 36 |
| Over 28 days | 1* | | 3 | | 4 |

* This patient had an 8-weekly cycle

most observers, considers that both types of uteri are hypoplastic, hence the dysmenorrhoea. However, it would seem more logical to conclude that since the constant feature of both types of uterus is the shape

There were 4 patients whose endometria showed small and inactive glands and the pathological reports contained a reference to possible atrophy. In each case, however, it transpired that the curettings were taken

within 1-2 days of the cessation of menstruation and their appearance was not inconsistent with a diagnosis of an early proliferative phase. Curettings taken between the 14th and 20th days of the cycle are reported as proliferative or pregravid in about equal numbers. This is to be expected in view of the natural variation in the time of onset of progesterone effects and also because a doubtful early secretory reaction was not accepted. There were only 2 instances in which the histological picture did not conform to the phase expected according to the stated date of the last menstrual period. In these ((a)—Table IV) the endometrium showed hyperplasia and not any sign of secretory activity in the last week of the cycle—indicating an anovular cycle. Apart from these 2 cases our findings support the view that menstruation characterized by pain is of the ovular type. Bickers⁶ in his enquiry into 17 cases of dysmenorrhoea found endometrial evidence of ovulation in every case. But Lackner and others¹ found one exception in their cases. However, in a large series of cases it is only to be expected there are exceptions to this rule because of the many possible factors contributing to dysmenorrhoea. But if the part played by the corpus luteum in the etiology of spasmodic pain is as important as other evidence goes to show, then it is surprising that Hoffman¹⁰ found that only two thirds of his patients showed a secretory endometrium in the second half of the menstrual cycle.

To conclude, in this series of 829 cases of spasmodic dysmenorrhoea, definite evidence of uterine hypoplasia was found in 15 cases only; and in a further 12 there was some evidence according to examination findings and menstrual history although the length of the uterus was not recorded as less than normal. At most there were only 27 patients (3.38 per cent) with a hypoplastic uterus. Our findings are con-

trary to those of numerous writers who variously estimate the incidence of hypoplasia as 20 to 100 per cent. They conform more closely with the reports of Gemmell²⁸ and Davis¹⁴ who found hypoplasia in only 10 per cent cases. Moreover it should be remembered that even when hypoplasia is found it is not necessarily the cause of the dysmenorrhoea and so Davis expresses doubt as to whether, in his 10 per cent cases, the hypoplasia had much etiological significance.

OTHER CONSIDERATIONS.

So far it has been demonstrated that according to the limited *data* available, hypoplasia of the uterus was an infrequent finding in this large series and even in the few cases in which it occurred there is nothing to prove that the hypoplasia in itself was a causal factor of the dysmenorrhoea.

But it is extremely difficult to present irrefutable evidence and it will remain difficult so long as the diagnosis of hypoplasia remains more or less a matter of individual opinion. Apart from the negative evidence provided by this series there are further points which merit discussion.

(1) *Age of onset of dysmenorrhoea.*

Spasmodic dysmenorrhoea often does not commence until a few years after the menarche, or, if present in slight degree at puberty, only becomes intense at a later age. The age at which the patient seeks advice is a good guide to this feature and Davis¹⁴ found that the average age of patients seeking treatment for dysmenorrhoea (congestive and spasmodic) was 22.3 years, that is, about 7 years after the average age for the menarche. In our series of spasmodic dysmenorrhoea cases the ages of the patients at the time of treatment is shown in Table V.

It will be seen that the ages of the majority of patients fall between 18 and 28, implying a considerable interval between the menarche and the development of pain of such severity as to demand hospital treatment. For further evidence of this we

importance from the standpoint of this thesis. It has been suggested by Moir,¹² Sturgis and Albright⁹ and others, that the reason for it is that, in the early years, menstruation is anovular, and it is only when the ovaries function fully and ovu-

TABLE V.

| Age | Below 15 years | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 |
|--------------|----------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| No. of cases | 2 | — | 18 | 31 | 57 | 51 | 54 | 55 | 58 | 58 | 49 | 43 | 47 | 48 | 49 |

| Age | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | ? |
|--------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|---|
| No. of cases | 36 | 37 | 22 | 31 | 24 | 15 | 15 | 8 | 7 | 8 | 3 | 1 | — | — | 1 | 1 |

have analysed the case histories of 457 patients of our series; the remainder are excluded because the details of the time of onset of dysmenorrhoea are not stated. The findings can be summarized as follows:

| | |
|--|-----------|
| Onset of pain one or more years after menarche | 240 cases |
| Slight pain at menarche becoming severe one or more years later ... | 34 cases |
| Pain dating from the menarche. (In some of these cases it is possible that the pain at puberty was only slight, becoming more severe later) | 183 cases |
| Total | 457 cases |

It will be seen that approximately 60 per cent (274 out of 457) experienced at least one year of painless menstruation or only slight dysmenorrhoea before developing incapacitating pain. The figure is rather higher than those given by other observers; thus the estimates of Novak and Reynolds,⁶ and Randall and Odell,²³ are 42 per cent and 35 per cent respectively. But the age at which dysmenorrhoea asserts itself is difficult to compute and, no matter what the exact percentage may be, all writers are agreed that an interval between onset of menstruation and the onset of dysmenorrhoea, is common, and it is usually 2 to 4

years in duration. This time-lag is of some late that dysmenorrhoea shows itself. This view is supported by the fact, previously mentioned, that the presence of a corpus luteum would appear to be essential for dysmenorrhoea. Nevertheless, it is unlikely that anovular menstruation is constant even though it be common in young girls, and in that case one would expect them to have intermittent dysmenorrhoea, gradually becoming a constant feature as ovulation becomes more regular. Such is not the rule although there are exceptions. Moir's theory may be correct but another possible explanation comes to mind and follows what has already been said about the development of the uterus. The interval between the menarche and the onset of dysmenorrhoea coincides with the interval between full anatomical development of the uterus and the time when it is "matured" and capable of full reproductive function. If there is any significance in this coincidence then it would seem that dysmenorrhoea is evidence of complete rather than incomplete development. This is all the more logical if it be remembered that, in subjects of dysmenorrhoea, the severity of the pain is to some extent related to the strength of the uterine contractions. A well-developed muscle is likely to contract more forcibly than a hypoplastic one.

Another feature of the age of patients suffering from dysmenorrhoea is the fact, noted by all observers, that the pain tends to improve after the age of 30, and spasmodic dysmenorrhoea is rare after the age of 35. As mentioned previously, underdevelopment of the uterus is closely allied to atrophy, since both are dependent on the same cause—lack of the oestrogen stimulus. Atrophy is undoubtedly associated with a loss of muscle tissue and an increased proportion of fibrous tissue. If, therefore, one of the characteristics of hypoplasia is an excessive amount of fibrous tissue and it is this which causes painful contractions, why does not dysmenorrhoea commence as atrophic changes set in with advancing years? In fact a woman approaching the menopause rarely, if ever, suffers spasmodic dysmenorrhoea.

(2) *Fibrous Tissue in the Uterine Wall.*

The occurrence of a high proportion of fibrous tissue in the uterine wall should have the effect of weakening uterine contractions and, contrary to the usual statement, reason would suggest that pain would be less likely to result. In any case there is no evidence to show that fibrous tissue does cause dysmenorrhoea and we have failed to find in the literature any convincing account of the microscopic demonstration of an undue amount of fibrous tissue in uteri which have been the seat of menstrual pain. Observations, for the most part, have been made on isolated specimens only. Schultz,³⁰ who is reputed to be the originator of the theory, did not support it with histological data. However, in 1912 Schickele and Keller,⁵³ who studied sections of the myometrium in a series of cases, concluded that there was no relation

between the amount of fibrous tissue present and the occurrence of dysmenorrhoea. It would appear, however, that these writers were more concerned with so-called "chronic metritis" and congestive dysmenorrhoea. Again there appears to be considerable difference of opinion as to what is to be regarded as the normal proportion of connective tissue in the myometrium at various ages.

The adherents of the fibrous tissue theory of dysmenorrhoea follow Schultz³⁰ in explaining the cure of the pain by pregnancy by assuming that pregnancy improves the development of muscle at the expense of fibrous tissue. However, according to Reynolds⁷ the most constant and permanent effect of pregnancy is an increase in the connective tissue elements in the myometrium. This is true to some extent during pregnancy and is obvious after pregnancy when a de-differentiation of muscle fibres takes place.

Nevertheless, it may still be argued that a patch of fibrous tissue, localized to some site such as the internal os, such as Blair Bell⁵² claims to have demonstrated in the cochleate uterus, might interfere with the contraction wave or in some way disturb the polarity of the uterus. Davis¹⁴ does not accept this because the painful contractions are essentially rhythmical without evidence of incoordination. This argument is not necessarily valid, however, because contractions may still occur at regular intervals even though the muscle wave is not co-ordinated from the standpoint of function. However, it should be pointed out that the presence of scars in the uterine wall, as after Caesarean section or myomectomy, although a theoretical cause of dysmenorrhoea, rarely have such an effect. And this is true even when the scar extends transversely at the level of the internal os, or isthmus, as after the lower segment operation.

* Unlike most writers, Crossen and Crossen⁶² consider that atrophy of the uterus in virgins over the age of 30 does sometimes cause dysmenorrhoea.

(3) *Size of the Uterus.*

Apart from the evidence given previously, it should be mentioned that several observers have commented that the uterus of patients suffering from dysmenorrhoea subjected to laparotomy never looks small or infantile in form. Conversely, many women with proved hypoplastic uteri do not experience dysmenorrhoea, and this is admitted by those who support the hypoplasia theory of dysmenorrhoea. Taylor,⁴⁵ in her recent clinical survey of 200 girls, came to the conclusion that a small uterus was found more commonly in the mild than in the severe grades of dysmenorrhoea. Mazer and Israel³³ make the interesting comment that uterine (and ovarian) hypoplasia associated with thyroid or pituitary hypofunction rarely causes dysmenorrhoea because patients suffering from such disorders are necessarily of phlegmatic disposition, insensitive to pain.

CASES OF UTERINE HYPOPLASIA.

The second part of our investigation consisted in a study of the case records of 86 consecutive patients whose uteri were proved to be undersized by a cavity measurement of less than 2½ inches. The difficulty in distinguishing hypoplasia from atrophy has already been mentioned and it should be emphasized that the finding of a small uterus does not necessarily mean that it has not once been fully developed and that it has not subsequently diminished in size and become inactive. In order to exclude as far as possible all cases of natural menopause, and of delayed puberty within physiological limits, only patients within the age limits of 18 and 40 are included. A further difficulty at once manifests itself—a large proportion of patients with proved hypoplasia or atrophy suffer from amenorrhoea and are therefore valueless from the point of view of a study of dysmenorrhoea.

Hypoplasia and atrophy result either

from lack of oestrogen or an inability of the uterus to respond to an oestrogenic stimulus. It might be supposed that once a uterus has been capable of response to oestrogens, it always remains so, and the atrophy therefore is always due to ovarian failure. Although this is ordinarily true, thus the post-menopausal uterus will nearly always respond, it is not always true and we know of a few cases of secondary amenorrhoea and uterine atrophy in which enlargement of the uterus and further uterine haemorrhage could not be produced by the exhibition of oestrogens. This is sometimes seen in the presence of general disease such as tuberculosis, and it may be that such clinical observations are accounted for by some circumstances inactivating or destroying the oestrogen (*vide supra*), rather than by loss of uterine reactivity. Prolonged oestrogen therapy might of course make the uterus refractory, at any rate for a time, but Mazer and Israel³³ say that the uterus may become insensitive after a long period of amenorrhoea. It seems unlikely, however, that uterine inactivity alone could have this effect and the suggestion is not borne out by cases which we quote later.

It is doubtful whether it is permissible to assume that the endometrial response by haemorrhage, and the myometrial response, of a uterus, follow a similar pattern, although most of the available evidence shows that they do, at least in the majority of cases. In our enquiry into cases of hypoplasia we have therefore assumed that such is the case and a uterus which cannot be made to bleed with oestrogens is presumed to be insensitive to these principles in other respects as well.

We have attempted to assess the primary cause of uterine hypoplasia or atrophy in these 86 cases and our conclusions are shown in Table VI. In the section "uterus unresponsive" are included those cases in

TABLE VI.
Causes of Uterine Hypoplasia (or atrophy)
in 86 Cases.

| | Cases |
|--|-------|
| A. Uterus Unresponsive to Oestrogen ... | 21 |
| B. Endocrine Dysfunction. | |
| 1. Primary pituitary fault | |
| (a) Fröhlich's syndrome 8 | 23 |
| (b) Simmond's syndrome 5 | |
| (c) Cushing's syndrome 2 | |
| (d) Infantilism 4 | |
| (e) Gigantism 2 | |
| (f) Partial pituitary failure following pregnancy 2 | |
| 2. Primary ovarian fault. | |
| (a) Premature menopause 3 | 5 |
| (b) Eunuchoid syndrome 2 | |
| 3. Primary thyroid dysfunction ... | 1 |
| 4. Primary adrenal cortical dysfunction | 2 |
| 5. Endocrine disturbance ?Primary in ovary ?Primary in pituitary ... | 12 |
| C. Endocrine Dysfunction or Unresponsive Uterus or Both | 12 |
| D. General Disease. T.B., anaemia, etc. | 4 |
| E. Anorexia Nervosa or Hysteria ... | 3 |
| F. Environmental Factors | 3 |
| Total | 86 |

which uterine response, as judged by withdrawal haemorrhage, could not be produced by oestrogens. In general, it can be stated that the smaller the uterus, the less likely it is to respond. Other clinical features are summarized in Tables VII, VIII, IX and X.

Our main concern has been to determine how many of these patients with small uteri suffered from spasmodic dysmenorrhoea. Sixteen patients had primary amenorrhoea and can therefore be omitted from consideration; 42 patients had secondary amenorrhoea and of these 3 gave a history of having had spasmodic dysmenorrhoea in the past. This finding however is of little significance since at the time they were menstruating the uterus may have been normal in size, atrophy and amenorrhoea having set in later. Twenty-eight patients were menstruating at varying frequencies and of these only one complained of severe dysmenorrhoea; 4 others mentioned dysmenorrhoea as a subsidiary complaint, while another 3 admitted having minor discomfort with menstruation, but of this they did not complain.

TABLE VII.
Age of Patients

| | | | | | | | | | | | | | | | | | | | | | | |
|--------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Age 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 |
| No. 9 | 10 | 10 | 5 | 4 | 1 | 5 | 1 | 2 | 5 | 6 | 6 | 6 | 0 | 5 | 1 | 3 | 1 | 0 | 4 | 1 | 1 | 0 |

TABLE VIII.
Age at Onset of Menstruation.

| | | | | | | | | | | | | | |
|-----|---------|----|----|----|----|----|----|----|----|----|----|----|-------------------|
| Age | Unknown | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | Never menstruated |
| No. | 2 | 2 | 3 | 2 | 10 | 18 | 15 | 8 | 5 | 3 | 1 | 1 | 16 |

TABLE IX.
Length of the Cavity of the Uterus.

| | |
|--|---------|
| Uterus rudimentary and not canalized ... | 4 cases |
| Less than 1 inch | 1 .. |
| 1 to 1½ inches | 3 .. |
| 1½ to 2 inches | 7 .. |
| 2 to 2½ inches | 36 .. |
| Less than 2½ inches, but exact measurement not recorded | 35 .. |

Judging by the statistics given by Pullen and Hamblen,¹⁷ Hoffman,¹⁰ Mazer and Israel,³³ Randall and Odell,²³ Miller,⁵⁴ Ehrenfest,¹⁹ Davis,¹⁴ Winther⁵⁵ 35-50 per cent of all women experience some menstrual discomfort, and 5-10 per cent experience incapacitating pain. So the incidence of dysmenorrhoea in this series is not above the average, and it could with

some justification be claimed that it is less than average. There is nothing to suggest, therefore, that hypoplasia in itself causes dysmenorrhoea.

Study of the age of the menarche and the subsequent menstrual rhythm in these cases raises some doubts about the validity of other traditional opinions about uterine hypoplasia. The high incidence of amenorrhoea conforms to the accepted view. If those

fault is always in the ovary, and the smallness of the uterus is merely a secondary effect, as is the symptom of infrequent menstruation.

The Use of Oestrogens in the Treatment of Uterine Hypoplasia.

So far we contend that this investigation provides little evidence to substantiate the view that uterine hypoplasia causes spas-

TABLE X.
Menstrual Function.

| | | | |
|-----------------------|----------|-------------------|---------|
| Primary amenorrhoea | 16 cases | Epimenorrhoea | 2 cases |
| Secondary amenorrhoea | 42 .. | Normal .. | 7 .. |
| Menstruating ... | 28 .. | Infrequent menses | 16 .. |
| | | Scanty menses | 3 .. |

patients with primary amenorrhoea are excluded, it can be seen from Table VIII that the age of the onset of menstruation quite often falls within the normal limits. Fifty out of 68 patients began to menstruate before their 16th, and all except 5 before their 18th birthday. A late menarche is not so constant a feature of uterine hypoplasia as many would have us believe. Among those patients who were menstruating, only 3 had scanty menstruation and this goes to show that the amount and duration of the flow bears no close relation to the development of the uterus and, incidentally, to the efficiency of the ovaries. Infrequent menstruation is common, however, and this is not surprising since the cycle reflects ovarian function and deficiency of the latter would account for uterine hypoplasia or atrophy.

It can be concluded that the menstrual disturbances which should lead the clinician to suspect uterine hypoplasia are amenorrhoea or infrequent menstruation; a late menarche may or may not be significant. In the case of amenorrhoea the fault may lie primarily in the uterus, or the ovary, but in infrequent menstruation, the

modic dysmenorrhoea, or at least that it is concerned in only a small percentage of cases. But for reasons already mentioned it is difficult if not impossible to prove it conclusively. Oestrogens are certainly responsible for the normal development of the uterus and for maintaining its integrity, and if spasmodic dysmenorrhoea is due to underdevelopment then oestrogen therapy, so frequently advised, is at first sight not unreasonable, in spite of the fact that a deficiency of oestrogen in the blood—or indeed any upset in the hormone level in the blood—has not been demonstrated (Fluhmann,¹⁶ Katz and Parker¹⁸).

Clauberg³⁹ claims to have demonstrated radiologically an increase in size of the uterus following oestrogen administration, and the experience of most clinicians is that a small uterus can often, but not always, be stimulated to full development, but the effect is usually a temporary one (Mazer and Israel³²). Nevertheless, Lardaro,⁵⁶ using stilboestrol in the treatment of 30 cases of infantile uterus, found that the size and consistence of the uterus were altered in 5 only. In 3 of these the effect produced was temporary and Lardaro

concludes "except in rare instances, the drug does not produce any demonstrable enlargement of the uterine cavity." Kaufmann (quoted by Ehrenfest¹⁹) also found that, in cases of uterine hypoplasia associated with primary amenorrhoea, the uterus rarely responded to oestradiol benzoate. The effect of oestrogen therapy depends on the inherent ability of the uterus to react in any given case: if the uterus is sensitive and its hypoplasia caused by oestrogen deficiency, then the administration of oestrogen results in its full development. This effect is temporary, however, and the uterus quickly returns to its former state when treatment is suspended. Moreover, oestrogens inhibit the function of the ovaries so these may eventually be less able to maintain the uterus in its fully developed state. Again this type of replacement therapy cannot be continued successfully for an indefinite period, for after a time it ceases to have any stimulating effect on the uterus and atrophy sets in. It may be argued and indeed has already been suggested by Lane Roberts and others⁴⁰ that, when uterine hypoplasia is considerable in degree, then the giving of oestrogen may be necessary to assist the ovaries in producing full development which, once attained, can be supported by the ovaries even when their function may be somewhat subnormal. This view presupposes that more oestrogen is required to develop the uterus than to maintain its integrity and function and yet there is no evidence that this is so. In fact uterine development normally proceeds apace at a time when the ovaries have not yet assumed their full activity. It would seem more reasonable to postulate, as do Allen and others⁵⁷ in respect of the endometrium, that a higher output of oestrogen is required to maintain the uterus in a state of full development than to stimulate its development over a period of time. In regard to this aspect of

the subject we should like to quote a recent experience with a patient (included in our second series) who suffered from an androgenic adenoma of the adrenal cortex and at the age of 30 presented the classical features of the adrenogenital syndrome, features which had gradually developed since the age of 14. She had never menstruated and at laparotomy the uterus was found to be about the size and shape of the uterus in infancy. It was so small and thin that it could not be palpated on bimanual examination under general anaesthesia. The ovaries contained numerous atretic follicles, ovulation and ovarian activity having been suppressed by a very high androgen output by the tumour. After the tumour had been removed it was at first thought—in line with current opinion—that the administration of oestrogens would probably be necessary in order to bring the uterus to full development, before it could be expected that the ovaries themselves could commence a regular menstrual cycle. Nevertheless, such treatment was deliberately withheld and, within 8 weeks, the uterus increased to normal size and the patient began to menstruate and thereafter had a regular cycle. The cure of primary amenorrhoea at the age of 30 is a striking feature of this case, but what is even more remarkable is the demonstration of the ability of the ovary, when allowed to function normally, to promote full uterine development, even at a late age. And yet how often has it been stated that it is difficult, if not impossible, to cure uterine hypoplasia once the patient has reached the age of 20. Meaker⁵¹ says that after 20 years the growth impulse is lost and he supposes that the cause of hypoplastic uteri seen in women with a normal menstrual cycle is a transient glandular derangement in youth. This idea, which receives constant support, and often leads to the premature treatment of what is only a slightly delayed

but otherwise normal puberty, has no foundation if the concept of uterine development as set out here is true. Our interpretation of the facts known at present is that if the ovary is capable of ovulating and of stimulating the uterus to menstruate, then it is capable of promoting full development of the uterus. And this is true at any age providing the uterus is sensitive, and providing that there is no factor resulting in oestrogen destruction. Any endocrine derangement resulting in temporary hypofunction of the ovary does not permanently impair the ability of the uterus to develop and if, at a later date, ovarian function is sufficiently restored to produce menstruation, then the uterus will also attain adult proportions.

One further feature of the case quoted above deserves mention. During her first few menstrual periods the patient did not experience any pain, but after 3 or 4 months, the patient began to complain of moderately severe spasmodic dysmenorrhoea. In other words the onset of dysmenorrhoea coincided with full development and not the reverse; or it may be, if Moir's theory is correct, that the initial bleedings were anovular and only when the ovarian cycle was fully established, with corpus luteum formation, did the patient experience pain.

Another interesting case is quoted by Pratt.⁵⁸ A girl of 17, having previously menstruated regularly, adopted a strictly limited diet to reduce her weight and, as a result, developed secondary amenorrhoea and uterine hypoplasia (more strictly atrophy) which lasted 10 years. After marriage and a return to normal diet, the condition corrected itself, menstruation became regular, the uterus normal in size, and a pregnancy ensued. And there must be many cases of this type, showing that suppression of ovarian function for many years does not interfere with the uterus

assuming or resuming its normal proportions and functions, once the ovarian cycle is established or re-established.

But what of those patients whose ovarian function is adequate and in whom hypoplasia is the result of uterine insensitivity to hormones? In such cases oestrogen therapy is only rational if it can be shown that the insensitivity of the uterus can be overcome by increasing the level of hormone in the blood above the normal. Our comments on postpubertal development include reference to the possibility that full functional capacity may be dependent on exposure of the uterus to stimuli from repeated ovarian cycles, but so far as we are aware there is no definite experimental proof that an oestrogen influence does make the uterus more sensitive to this hormone; opinions vary. Mazer and Israel,³³ dealing with amenorrhoea, say that in those cases in which the uterus initially will not respond by oestrogen withdrawal haemorrhage, treatment should be continued for a period in the hope of increasing its sensitivity, but they point out that failure is common. The same authors, referring to pituitary disease, say "oestrogen is valuable in combating the uterine atrophy and in increasing the responsiveness of the uterus to improved ovarian activity obtained through other measures."

Clauberg⁴⁹ maintains that both the animal and human uterus, after being subjected to the influence of oestrogen, responds better to that hormone than does the infantile one. However, Moricard⁵⁰ says quite definitely that the administration of oestrogen to patients whose own oestrogen production is normal, does not have any good effect on a hypoplastic uterus. Lane Roberts and others⁴⁰ suggest that oestrogen therapy does influence uterine hypoplasia, even in those patients with normal hormone levels, but they conclude that in such cases the ovaries are under-

active rather than inactive. They do not claim that uterine sensitivity is increased, and indeed point out that the reactivity of the uterus develops in spite of the absence of ovarian activity. The only proved effect of oestrogen on uterine reactivity is the depression which follows prolonged administration. On the evidence so far available it is not permissible to conclude that the sensitivity of the uterus to oestradiol produced by the patient's ovaries, is increased by the administration of other oestrogens. If it were so, the uterine effects of oestrogen therapy which has been practised so widely in recent years, would have been more permanent.

If this conclusion is correct then uterine hypoplasia which exists in spite of normally functioning ovaries cannot be effectively treated with oestrogens and this applies no matter whether the patient's symptoms are amenorrhoea, dysmenorrhoea or sterility.

On the other hand, if the uterine hypoplasia is secondary to ovarian hypofunction, then the administration of oestrogens is equally valueless from the point of view of a cure; unless the ovarian fault is corrected sterility will persist in spite of a temporary increase in size of the uterus, and amenorrhoea will return as soon as treatment is suspended. This is not to deny the administration of oestrogen any place in the management of cases of uterine hypoplasia. But it should be employed as a diagnostic measure—to determine, by its intermittent application over a period of 1 to 3 months, whether the uterus is capable of response, and thus to assist in the diagnosis of the underlying cause of the hypoplasia or atrophy.

If uterine hypoplasia rarely if ever causes dysmenorrhoea, and if in any case oestrogenic hormone therapy is of no value in producing permanent, and in many cases even temporary, enlargement of the

uterus, then how can we account for the reports^{9, 23, 24, 25} of good results attending oestrogenic hormone therapy for spasmodic dysmenorrhoea. This has recently been discussed by Pullen and Hamblen¹⁷ and there are many possible explanations.

1. Oestrogens may exert an effect on dysmenorrhoea by increasing the vascularity of the uterus, thus counteracting to some extent the ischaemia which is possibly an important factor in the causation of the pain. Also the contractions resulting from oestrogens as distinct from those due to progesterone tend to promote a better uterine circulation (Reynolds³⁹).

2. Dysmenorrhoea does not occur except in the presence of progesterone. If oestrogens are administered in the first half of the cycle, ovulation and corpus luteum formation may be inhibited and the ensuing menstruation will be anovular and therefore painless. Sturgis and Albright⁹ and Bickers¹¹ claim to have demonstrated by clinical experiment that when oestrogens relieve dysmenorrhoea, this is the mechanism involved. If oestrogens are given after ovulation they may still act by depressing corpus luteum activity. In assessing this view, it should be remembered that oestrogen has been shown to promote corpus luteum formation and to influence its function favourably (Hoffman,¹⁰ Fevold,⁶⁰ Allen and others⁵⁷).

3. It has been suggested that oestrogens may affect the central nervous system raising the threshold for pain.

4. Oestrogens may counteract the degenerative change in the paracervical nerve ganglia. Kennedy²¹ first demonstrated these changes as a feature of dysmenorrhoea and claims to have shown that they can be counteracted by oestrogens.

5. By promoting growth, softening, and vascularity of the cervix, oestrogens may help to restore uterine polarity to normal, or again it has been suggested that oestro-

gen tends to co-ordinate uterine contractions, progesterone having an opposite effect.

6. One of the effects of oestrogens is the liberation of acetylcholine or some similar substance and this, by acting on parasympathetic nerve endings, may influence either vascularity or the neuromuscular mechanism (Reynolds^{7, 61}).

It has still to be proved that oestrogen does have any specific effect on spasmodic dysmenorrhoea. Bishop⁶² estimates that reports in general indicate relief of symptoms in 50 per cent cases, although the effect is temporary (^{3, 33, 34, 35}). But it is not difficult to find claims for equally good results for all manner of treatments—progesterone, testosterone, gonadotrophin, general hygienic measures, psychotherapy, desensitization, various drugs and operative procedures. The nervous factor is so important in dysmenorrhoea that any treatment acting psychologically will yield a good percentage of cures. It is perhaps significant that in regard to oestrogen therapy some of the best results were reported by the earlier workers (e.g. Kennedy²¹) and were obtained with preparations which we now realize contained relatively small amounts of oestrogenic principle. Moreover Winther^{55, 63} has recently reported a series of 100 cases of dysmenorrhoea in university students and shows that the results obtained with emmenin (oestriol) were no better than those obtained in the control series treated with a placebo. Hoffman¹⁰ says his experience is similar. There is therefore good reason to doubt whether oestrogen therapy has any special value in the treatment of dysmenorrhoea; if it has, and it acts by any of the mechanisms above, then its effect must still be a temporary one. These possible modes of action should be kept in mind when it is employed.

SUMMARY.

1. The pain of spasmodic dysmenorrhoea is related in some way to contractions of the uterus. The difference between painful and painless contractions lies in their character rather than their strength. The particular pattern of uterine motility causing pain during menstruation is unknown but the view which supposes inco-ordination of different areas of the uterus, or disturbed polarity of the uterus, has still to be disproved.

2. The theory which supposes uterine hypoplasia as the cause of the abnormal uterine contractions, and the evidence on which it is based are critically examined in the light of what is known about the development of the uterus.

3. An analysis of the histories of 829 patients suffering from spasmodic dysmenorrhoea shows:

- (a) Not more than 27 patients had definite signs of uterine hypoplasia.
- (b) The age of the menarche was usually within normal limits.
- (c) Scanty and infrequent menstruation was exceptional and most women had a regular cycle.
- (d) Endometrial studies in 111 cases showed, with 2 exceptions, that the histological phase agreed with the time in the menstrual cycle. Painful menstruation is usually ovular in type.
- (e) 457 patients had some minor malformation or malposition of the uterus, but these faults are not accepted as an indication of hypoplasia.
- (f) The existence of an interval between the menarche and the onset of dysmenorrhoea in a large percentage of cases is confirmed. This in itself is evidence against the hypoplasia theory.

4. An analysis of a second series of 86 patients, all of whom had a hypoplastic or atrophic uterus, shows that of the 28 women who were menstruating only one had dysmenorrhoea of an incapacitating degree.

5. The effect of oestrogen on a hypoplastic uterus depends on the ability of the organ to respond. If the uterus is insensitive then oestrogen therapy is useless. If, however, the uterus is sensitive then there is no point in increasing its size temporarily unless the cause (usually ovarian under-activity) is corrected. Furthermore, if the cause is successfully treated, the hypoplasia is automatically cured and oestrogen is unnecessary.

6. The value of oestrogen therapy in spasmodic dysmenorrhoea is open to question. If it does give relief, albeit temporary, then it does not necessarily do so by overcoming hypoplasia. Several other possible modes of action are listed.

7. Throughout this paper we have deliberately adopted a critical and provocative attitude. The evidence is insufficient to prove or disprove the hypoplasia theory of dysmenorrhoea and it will remain so as long as the pathology of uterine hypoplasia is in doubt and its diagnosis depends on the opinion of individual clinicians. By setting out the facts as we see them we have endeavoured to draw attention to the need for a careful appraisal of the diagnosis and significance of uterine hypoplasia and atrophy, and for a sober outlook on the possibility of its successful treatment with oestrogens.

In conclusion we should like to express our indebtedness to the members of the Honorary Staff at the Women's Hospital, Liverpool, who have willingly allowed us to study and utilize the records of their patients.

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The Uncomplicated Primigravid Breech

A Technique Used in a Series of 60 Cases.

BY

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A SERIES of 60 cases of primigravid breech presentations delivered vaginally is presented. They constitute a consecutive series of cases delivered personally at Dilston Hall Maternity Hospital, Northumberland (48 cases); at Stagshaw House Maternity Hospital, Northumberland (6 cases); and St. Helier County Hospital, Carshalton Surrey (6 cases). The series, though small, has added interest in that it was conducted with a definite plan of campaign and carefully considered technique.

For the purposes of this series I have defined the uncomplicated primigravid breech case as occurring in a woman pregnant of a live baby weighing 5 pounds 8 ounces or over and having neither (a) multiple pregnancy, (b) placenta praevia, (c) gross prolapse of the umbilical cord, (d) accidental "toxic" haemorrhage, (e) eclampsia nor (f) monstrosity. Two cases of grossly contracted pelvis are not included in this series, both having been delivered by Caesarean section. One of these was an elective section for severe flat pelvis—patient aged 33—the other, an emergency admission, had a lower segment section for obstructed labour, the breech not being engaged after 4 hours at full dilatation with membranes ruptured for many hours and an awkward android pelvis. Caesarean sections were not performed for elderly primiparity. All cases available, whether booked, unbooked or emergency, have been included.

The result of 60 vaginal deliveries in

uncomplicated primigravid breech cases was 1 stillbirth and no neonatal deaths.

GENERAL DISCUSSION.

The disastrous results in vaginally delivered primigravid women have been frequently publicised in America and Britain by de Normandie, Schwartz, Irving, Goethals, Gibberd, Moir and others. The whole literature was adequately reviewed by Racker,¹ and it is not proposed to recapitulate it. The great volume and authority of this propaganda has had two marked effects in the last 10 years; first there has been a movement towards breech extraction under full anaesthesia and second, there has been increased employment of Caesarean section especially in private practice. Goethals,² working on a special assignment at Boston Lying-in Hospital, delivered all breech cases, primigravid and multigravid, by breech extraction under full anaesthesia. The results have been excellent and in the past decade they have reduced the foetal loss in mature breech cases to 5 per cent. These, of course, are men of unparalleled experience working with expert anaesthetists who can assure genuine full surgical anaesthesia with minimal anoxia of the foetus. The process of training assistants and juniors to their high degree of skill is likely to be costly in foetal life and few aspirants may succeed in equalling the masters. The necessity for full anaesthesia alone must weigh against the baby especially after long

labour and possible intrapartum sedation. Schwartz, quoted by Goethals, compromised by recommending that all complete and footling breeches should be delivered by extraction under anaesthesia, leaving frank breeches to spontaneous delivery with minimal manual aid.

The practice of performing Caesarean delivery for the uncomplicated breech with an adequate pelvis is to be deplored. Recent writers have widened their indications for abdominal section even to the extent that a primigravida over the age of 30 is classed as "elderly." I find that I am now asked by general practitioners to perform Caesarean section on their primigravid breech cases for the thinnest of indications, as age, nervousness, hard perineum, hypertension, absence of husband on war service, apparently regardless of the fact that the maternal risk of an abdominal delivery is at least 5 times that of a vaginal delivery. Neither should it be forgotten that many patients, for reason of fear or expense, commit themselves to what can be called One-child Caesarean Sterility.

This paper is written to show that there is another side to the medal. An increasing number of satisfactory series has been reported and reasonable figures are being turned out both in public and private practice. Marshall³ reported a series of 36 normal primigravid breech cases with 1 loss. Macafee and McClure⁴ have reported a foetal loss of only 4.84 per cent in a corrected series of booked primigravidae. The Simpson Memorial Hospital Report for 1942⁵ shows a corrected, booked primigravid foetal loss of 5.8 per cent. Urnes and Timerman,⁶ reporting the practice of the Chicago Lying-in Hospital district cases, showed a corrected foetal loss of 6.6 per cent for all breeches—these cases were delivered in the patients' homes by junior officers using local pudendal anaesthesia and aiming at spontaneous delivery. Pat-

ton and Mussey⁷ report a foetal loss of 5.34 per cent for uncomplicated primigravid cases. The best series I have been able to find is that reported by Hansen.⁸ With H. S. Morgan he has personally conducted a series of 64 uncomplicated cases. Their treatment has been extremely conservative and appears to have been minimal manual aid applied only when labour has been held up. They lost 1 baby in the 64 uncomplicated cases. In the same period 48 multiparae (uncomplicated) were delivered without any loss. Their conservatism is illustrated by the fact that the longest 1st stage of labour was 57 hours and the longest 2nd stage was 7¼ hours. In 126 total deliveries they employed manual aid 109 times, extraction 13 times and Caesarean section 4 times. Only 2 Caesarean sections were employed for elderly primigravidae with large babies, each weighing over 9 pounds.

Tompkins⁹ reports a unique series collected over 10 years from the Philadelphia Lying-in Hospital. From the records of 1,400 breech cases he selected *every case personally delivered* by 17 obstetricians "certified" by the American Board of Obstetrics and Gynecology. The resultant series of 211 cases was "corrected" by subtracting the premature infants, monstrosities, severe toxæmias, placenta praevia cases, twins and Caesarean sections. In the "corrected" series of 146 cases, there were only 4 babies lost—a mortality-rate of 2.7 per cent. When a further correction was made to include private patients only there were 2 losses in 139 cases. He does not extract the figures for primigravidae only. In the total of 211 cases it is noted, however, that there were no less than 31 cases delivered by Caesarean section. The technique is not described but in general it seems that the patients are "fully anaesthetized" before delivery.

It would appear, therefore, that vaginal delivery of the breech case can be made to give satisfactory results. The three outstanding series by Marshall, Hansen and Tompkins show good results by different methods. The common factors in their success are a good psychological approach, careful preliminary study, a definite, reasoned programme, and the ability at any moment in any case to carry out a smooth extraction when this is demanded.

METHOD OF DELIVERY.

The physician confronted with an uncomplicated primigravid breech case has the choice of 3 methods of delivery:

1. Caesarean section.
2. Breech extraction with full anaesthesia.
3. Spontaneous delivery with minimal manual aid.

(1) *Caesarean Section.*

It is obvious that there must be a greater place for Caesarean section for a breech presentation than for a vertex presentation in the primigravida. Trial labour is completely eliminated. The borderline case, particularly with trouble in the mid-pelvis or at the outlet, must receive the benefit of elective section. Full examination of the pelvis, if necessary under an anaesthetic, is indicated. Radiography with pelvimetry can be used to check clinical findings.

Caesarean section should also be elected when the baby is obviously large. The mortality-rate for babies over 8½ pounds rises very steeply.^{1,2} The combination of elderly primiparity and large baby is not uncommon.

Elderly primiparity by itself should seldom lead to Caesarean section. A great deal depends on the state of "ripeness" of the cervix at the time of the onset of labour. In my experience the condition of the lower

uterine segment, cervix and upper vaginal tissues are of much greater importance than the perineum. The resistance of the last can largely be eliminated by anaesthesia, stretching and episiotomy. The combination of a thick, tubular, unripe cervix, hypertension and a longish period of sterility, with or without obesity, strongly indicates Caesarean section.

One last group of cases also merits abdominal section—cases with premature rupture of membranes, a high unfixed breech and a closed elongated cervix without early onset of effective labour. A final verdict on this type of case should be made before the membranes have been ruptured for over 24 hours.

(2) *Breech Extraction.*

Breech extraction can be elected for all breech cases as in the practice of Irving, Goethals and Potter. Excellent results can be obtained by the very experienced operator working with a skilled anaesthetist. Failure is most likely to be due to insufficient ironing-out of the perineum and lower vagina or inadequate anaesthesia. Gas and oxygen are insufficient and the more depressant anaesthetics must be used in full dosage. It should be remembered that the mother, particularly the exhausted or toxic mother, may not be fit for this ordeal, and the effect on the baby should also be considered. Every operator approaching any breech delivery may be called on, at any time, to make a breech extraction for such indications as arrest, foetal distress, constriction ring or prolapse of the umbilical cord; but that is a very different matter from deliberately planning a dangerous and exacting operation for a series of cases, at least 90 per cent of which could terminate spontaneously or with minimal manual aid.

(3) *Spontaneous Delivery with Manual Aid.*

The ideal delivery is spontaneous. The majority of breech cases in multiparae can

be so delivered. It is interesting and instructive to leave such a breech delivery entirely to itself and, with the mother in the lithotomy position, to watch the crowning, the upward lateral flexion, the restitution, the downward flexion, the smooth but sudden rotation of the back upwards and birth to the umbilicus. The baby can still be left untouched. By the mother's expulsive effort aided by the baby's weight, delivery can proceed still further. The baby rotates a little, the body advances, the anterior scapula appears, slides downwards and inwards towards the spine and often the arm and hand appear spontaneously. The body restores itself again and the other scapula appears laterally to be followed by arm and hand. The baby, still left untouched, hangs by the head in the Burns-Marshall position, the neck elongates, showing that the head is in the pelvis, and all that is left is to elevate the body and lift the head off the perineum. In the majority of multiparous cases the breech delivery is quicker, smoother and less painful than vertex delivery.

The problem, as it appears to me, is how to make conditions in the primigravida approximate to the delivery in multiparae: (a) how to get the uterus into full activity at the proper moment, (b) how to have the cervix fully dilated and withdrawn, (c) how to reduce the barrier of the vulva and perineum, (d) how to deliver the arms with minimal handling of the baby, and (e) how to reduce trauma in delivering the head. In my own series of 60 cases, I have performed breech extractions 5 times only. All the other patients have had minimal and very late manual aid. Recently I have been able, in most cases, to keep my hands off the baby entirely until the first scapula has appeared. In reaching this limit of non-interference, I have found the greatest assistance from the following technical lines.

- (a) Preparation of the patient.
- (b) Perineal and pudendal nerve block.
- (c) Preparation of vulva and perineum by "ironing-out." This is followed by posterolateral episiotomy.
- (d) The Lövset technique of delivery of arms.
- (e) A short rest in the Burns-Marshall position.

(a) *Preparation of the Patient.* Defective uterine action is very common among primigravidae. This accounts for a large proportion of instrumental deliveries in normal, as well as in occipitoposterior vertex cases. It has to be avoided as far as possible if the breech delivery is to be near-spontaneous. Prophylaxis begins early. The patient need not be informed of the breech presentation, or if she is aware of it, the import of it can be minimized. She is examined soon after the onset of labour with special attention to the condition of the cervix. If the cervix is fully ripe, thin and well taken up, mild sedation by heroin, pethidine, or by an opium-chloral-bromide mixture will probably suffice. If the cervix is still a thick tube, sufficient heavy sedation by morphine-scopolamine is indicated to ensure at least one good sleep. If the patient has had a few wakeful nights with prodromal signs of labour, intramuscular paraldehyde (10 c.c.) is well worth adding.

Later, one may attempt to regulate disordered or poor uterine action by calcium gluconate, oestrogens or intravenous glucose. In brief, one tries to bring the patient into the best possible condition when full dilatation is arrived at. To this end, the patient is not encouraged to bear down until the perineum is being well bulged. It should not be assumed that because a foot or knee or even a buttock is showing that the cervix is fully dilated. Often it is not. Wait until the breech is really at the vulva and actively dilating it

before proceeding further—usually by this time the patient is badly wanting to bear down.

(b) *Perineal and Pudendal Nerve Block.* The perineum being now distended by the advancing breech, the patient is put in the lithotomy position, cleansed, disinfected and draped. Local anaesthesia is induced. The method is easily learned and can be found described by De Lee,¹⁰ Brentnall,¹¹ and Griffin and Benson.¹² I find that 100 c.c. of 0.5 per cent procaine is sufficient. The solution contains 1 in 200,000 of adrenalin, but this can be omitted.

(c) *Ironing-out: Episiotomy.* In a few minutes the patient is greatly relieved and the vulva and perineum are ready to be ironed out. This can be done slowly and leisurely as labour is usually temporarily checked, possibly by adrenalin effect, and the patient is no longer subject to involuntary bearing down. During this period of calm, the patient should now have it explained to her that a special effort is required of her and that she should bear down in a very determined manner when the signal is given. When labour is resumed, strong down-bearing takes place, the breech advances, and now considerably bulges out the relaxed perineum. When the breech is about to crown a postero-lateral episiotomy is made. If the episiotomy is well-timed the breech is delivered in a few seconds and immediately before this event is due I have found it useful to give 3 units of pitocin intramuscularly. In more than half of my cases the delivery of the baby from the birth of the buttocks to well past the umbilicus has taken place during one uterine contraction.

The baby is still not touched and there is no need to disengage the feet of the usual frank breech. The baby's weight comes into play and birth as far as the scapulae without any interference is common.

(d) *The Lövset Manoeuvre.* This manoeuvre, described by Lövset,¹³ enables one to extract shoulders and arms in nearly all spontaneous deliveries without intra-vaginal manipulation. In the case of a left sacral anterior, when birth is well past the umbilicus, the baby, carefully splinted between both hands applied along the whole length of its visible body, is drawn slightly downwards and towards the mother's right and at the same time rotated slowly in a counter-clockwise direction. In this way, while descending, the posterior shoulder becomes lateral or frankly anterior. When the scapula appears it is pushed strongly towards the spine with the free index finger of the right hand. Usually the elbow, shoulder and hand (in that order) appear from the vulva. The baby is then drawn towards the mother's left side with slight traction and a slow rotation is made clockwise so that the baby's retained shoulder, which had become posterior, is restored to its original anterior position. While rotating, the shoulder and arm nearly always appear spontaneously. The baby is then released and allowed to hang by the head for about 20 seconds.

(e) *The Burns-Marshall Position.* The Burns-Marshall technique is very effective in flexing the head and by its gentle weight traction it nearly always draws the head well into the pelvic cavity. It also has a most effective teaching value. There is no better means of teaching students and midwives that hurry has no place in breech delivery; this 20 seconds relief from tension and apparently nonchalant approach to the final step in delivery is a most pointed lesson. It is probably good for the obstetrician too.

In this series I have used the Mauriceau-Smellie-Veit technique for delivery of the head. This manoeuvre I apply only once. If there is failure to get immediate easy extraction, the baby's feet are taken over

by an assistant and the forceps are applied to the after-coming head. The forceps were used for the head in 17 of this series of 60 cases.

In the last 2 years I have abandoned general anaesthesia for delivery of the after-coming head. It is quite unnecessary with a good pudendal nerve block.

In the occasional event of failure to induce the head into the pelvis by the Burns-Marshall position, the Weigand-Martin technique as described by De Lee¹⁴ is used, followed by the forceps, applied after the head is well down.

WHAT TO AVOID.

It one has elected for a spontaneous delivery with minimal manual aid, the patient should be watched and nursed to this end. The final preparations of local anaesthesia, ironing-out and episiotomy, are not made until the breech is completely down and bulging the perineum. The episiotomy is made late to avoid blood loss. If the local anaesthesia has been made prematurely and if the uterus is sluggish, one can always wait for the ideal moment. If necessary the local anaesthetic can be repeated. The majority of mistakes arise from hastening matters when a buttock, foot or knee is just showing. The cervix may not be fully dilated and withdrawn. Hastening (or assisting) matters when the patient is not ready, leads to the old-style assisted breech delivery. Fingers, tapes or instruments are hooked into the anterior groin, later into both groins. Next the buttocks or legs are drawn down against resistance. The patient suffers pain, panics and struggles. The whole genital canal begins to feel like a recalcitrant sphincter. A rushed anaesthetic is induced, there is more straining, more spasm, the baby's body becomes whitened and limp from the shock of handling and traction, and is as good as dead before the arms have been secured—one

has been caught in the half-way house, in something which is neither a breech extraction under surgical anaesthesia nor a spontaneous delivery with minimal aid.

It may be that at any time the plan for a spontaneous delivery has to be abandoned; maternal exhaustion, uterine inertia or maternal nervousness with inability to co-operate may negative the plan. Harm will not have been done if the local anaesthesia, ironing-out and episiotomy have all been prepared. The patient can then have full surgical anaesthesia induced without haste, flooding her with oxygen the while. When the anaesthetist is ready, a deliberate breech extraction is made.

It is noted that Hansen attributes his brilliant results to waiting patiently for spontaneous delivery and interfering (or aiding) as little as possible. He quotes his longest 2nd stage as $7\frac{1}{4}$ hours. My own limit has been 10 hours—in the 60th case of this series. The mother was comfortable for the most part of the time having only weak, irregular contractions and the baby was in no way distressed by the long wait. Extreme slowness does not imply obstruction.

CLINICAL DETAILS OF THIS SERIES.

Sixty cases were delivered vaginally.

Fifty-five had spontaneous delivery with minimal aid.

Five cases had full breech extraction, the indications being:

- | | |
|--|---|
| (a) Impacted breech, arrested progress | 2 |
| (b) Cardiac disease | 1 |
| (c) Nervous patient | 2 |

Anaesthesia for Impacted Breech:

| | |
|--------------------------------|---|
| Full chloroform and oxygen ... | 3 |
|--------------------------------|---|

| | |
|---------------------------|---|
| Spinal anaesthesia | 2 |
|---------------------------|---|

Episiotomy. Every case had a postero-lateral episiotomy.

Forceps on aftercoming head applied in 17 cases (28 per cent).

Premature rupture of membranes occurred in 18 cases (30 per cent).

Duration of labour:

1st stage, average 14 hours. Longest 43 hours, shortest 3 hours.

2nd stage, average $1\frac{1}{2}$ hours. Longest 10 hours, shortest $\frac{1}{2}$ hour.

Maternal mortality. Nil.

Maternal morbidity. Nil.

Stillbirths 1. Died of cerebral damage, with depressed fracture of the posterior parietal bone. This case was misdiagnosed as a vertex until well advanced in labour. Pinard's manoeuvre and breech extraction were made under full anaesthesia after 42 hours in labour, marked by disordered uterine action. The baby weighed 9 pounds. This case should have had Caesarean section. This was the second case of the series.

Neonatal deaths. Nil.

Neonatal morbidity. One case appeared to have some cerebral irritation. It was admitted to Newcastle Babies' Hospital, made a good recovery and is now, at 12 months of age, regarded as a normal baby.

Birth injuries. One case of fractured left clavicle. The same baby had a temporary right Erb's palsy which was cleared up in a week. Both arms had normal function before it left at 18th day. It is believed that in this case the damage was done by the forceps which were badly applied.

Delivery of the arms. The 5 cases of breech extraction all required intravaginal manipulation to disengage the arms. The writer favours the Lövsset manoeuvre of rotating the infant's body so that the posterior arm is brought into an antero-lateral position when it is usually easily swept down by fingers introduced, over and beyond the shoulder, from the posterior aspect. The reverse rotation is then made to secure the second arm anteriorly.

In the remaining 55 cases of spontaneous delivery, only 6 cases were rated as difficult in so far as they did require high vaginal interference for delivery of arms and shoulders on orthodox lines. In the other cases the arms were practically completely disengaged by the Lövsset rotation alone. Nuchal positions of arms were not encountered.

Ages of patients. The range in ages was from 17 to 40. Both extremes had spontaneous delivery.

Ten patients were in the age group 30 to 34; 5 patients were in the age group 35 and over. All in these two age groups had spontaneous delivery.

Type of breech presentation. Two cases were footling breech; 3 cases were complete breech; 55 were frank breech.

SUMMARY.

1. Sixty cases of vaginal delivery of the uncomplicated primigravid breech are presented. Delivery was accomplished with 1 foetal loss. The last 58 cases were delivered without any foetal loss.

2. The wide use of Caesarean section for the uncomplicated primigravid breech is deprecated.

3. It is suggested that only two distinctly separate techniques are permissible—(a) Deliberate breech extraction under full anaesthesia and (b) Spontaneous breech delivery.

4. It is maintained that the common assisted breech delivery with induction of anaesthesia gradually brought in during delivery falls between the two methods and exhibits the virtues of neither.

5. The writer believes that fully 90 per cent of primigravid breech deliveries can be spontaneous.

6. A technique of spontaneous breech delivery is outlined.

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The Relation of Vitamin B₁ Deficiency to the
Pregnancy Toxaemias
A Study of 371 Cases of Beri-beri Complicating Pregnancy

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FOR many years it has been suggested that a causal relation exists between dietary deficiency and the toxaemias of pregnancy. During the first world war it was noted in Germany that the partial elimination of protein and fat from the diet of pregnant women was accompanied by a 50 per cent decrease in the incidence of eclampsia. It has been customary to ascribe this lowered eclampsia rate to the sparse intake of animal protein, but it has also been suggested by De Lee¹ that lack of meat forced the patients to resort to a diet containing relatively large amounts of vegetables, black bread, etc., and that their vitamin B₁ intake was correspondingly higher than usual. In 1935 Theobald² advanced his dietetic theory of the causation of pregnancy toxaemia, or what he preferred to call the "Atelositesis of Pregnancy." He ascribed the condition to a deficiency in calcium, iron, iodine and vitamins of the B and D groups, and produced striking clinical evidence of his contention.

In 1938 Siddall³ suggested that a deficiency in vitamin B₁ was the basic aetiological factor in the causation of the various pregnancy toxaemias. In his view the normal function of the pituitary body can only be maintained in the presence of an

adequate supply of vitamin B₁. In the non-pregnant woman a deficiency of the vitamin causes hypofunction of the pituitary body, followed by oedema, lowered blood pressure, disturbed carbohydrate metabolism, and the other characteristic features of beri-beri. In the pregnant woman Siddall's view is that vitamin B₁ deficiency results in over-compensation or malignant hyperfunction of the pituitary gland, thus producing the symptoms of toxaemia, such as oedema, nausea, vomiting, increased blood-pressure, disturbed carbohydrate metabolism, etc. Siddall suggested that an adequate and constant supply of vitamin B₁ should prevent and possibly cure the toxaemias of pregnancy. This new concept for the first time harmonized all the conflicting manifestations of the toxaemias of pregnancy.

H. Yasunami⁴ also gave vitamin B₁ treatment to patients with hyperemesis gravidarum, pre-eclampsia and eclampsia. The patients were not given any other treatment and usually recovered rapidly. He expressed his belief that the administration of vitamin B during pregnancy would prevent the toxaemias of pregnancy and that patients with existing pre-eclampsia would not develop eclamptic convulsions.

W. Spitzer⁷ and F. C. Irving,⁸ in further communications, have stressed the value of vitamin B₁ and the vitamin B complex in the treatment of hyperemesis gravidarum.

During the years 1938 and 1939⁷ an important study was made of the records of 5,022 pregnant women attending 10 London Hospitals. A dietary deficiency was found in more than half of the patients. In 1,530 primigravidae receiving vitamins and mineral supplements the toxaemia rate was 27.1 per cent as compared with a rate of 31.7 per cent in a control group of 1,512 primigravidae not receiving the supplement. The investigations into pre-natal diet at the Toronto General Hospital by Ebbs, Scott, Tisdall, Brown and others⁹ showed a pre-eclampsia incidence of 12.6 per cent in patients receiving a poor diet in comparison with an incidence of 9.1 per cent in the supplemented diet group and 7.8 per cent in patients receiving a good diet. By a good diet the authors specified: protein, 80 to 100 grm.; fat, 80 to 100 grm.; carbohydrate, 350 to 400 grm.; calcium, 1.5; iron, 0.020; iodine in iodised salt, together with vitamins A, 6,000 i.u., B₁ 500 to 1,000 i.u., B₂ 3 to 3.5 mg., C 50 to 75 mg., and D 500 to 1,000 i.u.

Further studies by Burke, Beal, Kirkwood and Stuart¹⁰ showed a statistically significant relation between prenatal diet and the course of pregnancy. In their investigations no mother whose diet during pregnancy was considered "good" or "excellent" had pre-eclampsia, while with a "poor" to "very poor" diet almost 50 per cent had pre-eclampsia.

W.C.W. Nixon,¹¹ in his recent Blair-Bell Memorial Lecture, further stressed the importance of an adequate diet during pregnancy. In a previous investigation, Nixon, with his co-workers Wright and Fieller,¹² found that in 9 patients suffering from eclampsia there was a significantly low urinary output of vitamin B₁ as

compared with normal control pregnant women. In these patients, also, the placenta was found to have a markedly low vitamin B₁ content. The authors found a highly probable correlation between sub-optimal intakes of thiamine and the incidence of pregnancy toxaemia, and suggested that vitamin B₁ might be of value in the treatment of eclampsia.

Williams and Fralin¹³ also observed that 84 per cent of a group of patients who presented a history of nausea and vomiting in early pregnancy had a vitamin B₁ intake definitely below the pregnancy standard of 600 units daily. These authors did not, however, feel justified in assuming that there was "any positive relationship between dietary adequacy and the occurrence of certain complications of pregnancy and childbirth."

Other writers, indeed, have seriously questioned the relation of vitamin B₁ to pregnancy toxaemia. F. J. Browne¹⁴ conducted an investigation on a group of 169 pregnant women, of whom 88 were treated cases and 81 were controls. The 88 treated cases received by mouth 3 mg. daily of vitamin B₁ during the latter half of pregnancy. Of these patients 7.9 per cent developed a blood-pressure of 140/90 or over (or a blood-pressure in excess of 130/70 with albuminuria) as compared with an incidence of only 4.9 per cent in the control series. The author concludes that, so far as the prevention of pregnancy toxaemia is concerned, no beneficial effect is obtained by supplementing the diet with vitamin B₁. Another study by R. Kapeller-Adler and J. A. Cartwright¹⁵ revealed that in 4 patients suffering from mild toxaemia of pregnancy there was no improvement under vitamin B₁ therapy, whereas in 3 cases of severe toxaemia the condition actually became worse. As the result of this unfortunate experience the authors stated their belief that the thera-

peutic use of vitamin B₁ in toxæmia of pregnancy should be discouraged.

The majority of recent clinical and experimental observations, however, would appear to support the belief that a definite relation exists between dietary deficiency and the toxæmias of pregnancy. There is a gaining weight of evidence that the deficiency is notably, if not specifically, one of vitamin B₁ intake. It has been known for a long time that there is a greatly increased need for vitamin B₁ during pregnancy. In 1927, Moore and Brodie¹⁶ estimated that rats require four times the amount of vitamin B₁ to ensure the successful conclusion of a pregnancy than they do at other times. McCance, Widdowson and Verdon-Roe¹⁷ found, in an investigation of 120 pregnant women, that all were receiving sub-optimal amounts of vitamin B₁. The estimated daily intake, even including patients from the higher income groups, varied from 209 to 454 i.u., as compared with an optimal daily intake of 600 to 900 i.u.

More recently Lockhart, Kirkwood and Harris,¹⁸ in a very interesting communication, have produced concrete proof of an increased quantitative requirement for vitamin B₁ during pregnancy. These authors studied the quantity of thiamine needed by their patients to produce the same excretion status on successive lunar months during late pregnancy and the early puerperium. They found that in the 10th lunar month of pregnancy a patient requires three times as much thiamine as in the non-pregnant state to reach the same excretion peak. They also found that approximately three times as much thiamine was required by mouth as by the intramuscular route to reach the same excretion peak in non-pregnant subjects, thus indicating the relative efficacy of the two common methods of administration. The authors conclude that the requirements for thiamine during preg-

nancy and lactation are three times as great as in the normal non-pregnant state.

During the years 1939, 1940 and 1941 the writers had an unusually favourable opportunity, in Hong Kong, of observing the course of pregnancy in a large series of patients who were suffering from vitamin B₁ deficiency. True beri-beri, or avitaminosis B₁, was found in many of these cases, and hypovitaminosis B₁, or "sub-clinical beri-beri," was probably present in a much larger number, although clear evidence was often lacking, save for the frequent existence of oedema of the legs. An investigation into the clinical significance of oedema during pregnancy was commenced by one of the writers in conjunction with Professor W.C.W. Nixon in 1937, and was continued by the writers of this paper from the end of 1938 up to the time of the Japanese occupation of Hong Kong in December 1941. The following extract from the Report of the Department of Obstetrics and Gynaecology of the University of Hong Kong for the year 1939¹⁹ indicates the lines upon which the investigation was proceeding:

The existence of avitaminosis B₁, or beri-beri, is a complicating factor which is always to be reckoned with in obstetrical practice in Hong Kong. A fresh table is added to this year's report in which certain details are given of 49 clinically obvious cases of avitaminosis. It will be noticed that in 2 cases avitaminosis B₁ was the immediate cause of death, and that in 4 other cases it was a contributory cause. Avitaminosis therefore ranks very high as a cause of maternal death in Hong Kong, being present as a primary or secondary cause in 6 out of the 17 deaths for the year.

Poverty, improper dietary habits and the additional strains imposed by pregnancy are all potent factors in producing vitamin deficiency. Clinical beri-beri is the result in only a minority of cases, but what may be termed sub-clinical beri-beri is present in a large number of patients. These patients live on a dangerous border-line, and many factors, of little consequence in themselves, may suffice to precipitate the patient into a condition

of clinically developed avitaminosis. It will be noticed that pregnancy toxæmia, in one form or another, is a complicating factor in a number of cases of avitaminosis B₁. The line of demarcation is one that is difficult to draw and it may still prove that deficiency of vitamin B₁ is a causative factor in the production of the toxæmias. The amount of pyruvic acid in the blood has been used as an index of vitamin B₁ deficiency, and investigations are proceeding along this line in the hope that this relatively simple biochemical determination may shed light upon the relationship between the toxæmias of pregnancy and vitamin B₁ deficiency.

An investigation into the clinical significance of oedema during pregnancy was commenced by my predecessor Professor W. C. W. Nixon, and may throw further light upon the problem just mentioned. During 1939 a special record was kept of all cases showing oedema and it is found that they may be classified into three main groups:

- (a) Those associated with pregnancy toxæmia,
- (b) Those associated with avitaminosis B₁, and
- (c) Those not accompanied by signs of either pregnancy toxæmia or avitaminosis B₁.

In this latter group there were 271 cases. In the vast majority of these the oedema was limited to the legs, and the duration varied from a week to 9 months, the average duration being 44.5 days. The oedema was, therefore, by no means a transient symptom. In some patients pressure was undoubtedly a factor in producing the oedema, as evidenced by the fact that there were no fewer than 9 twin pregnancies among the 271 cases. In other cases, however, it could not be claimed that pressure was a specially significant factor. In view of the frequency of the toxæmias of pregnancy (6.01 per cent of all admissions for 1939) and of avitaminosis B₁ (1.47 per cent of all admissions for 1939), in both of which conditions the presence of oedema is almost invariable, it is hard to resist the conclusion that, in many cases, the appearance of simple oedema may be only a preliminary to the development of the full manifestations of toxæmia on the one hand or of avitaminosis B₁ on the other, and it is not beyond the realm of possibility that all three are bound up in a common aetiology.

The year 1940 brought with it an increased incidence of beri-beri and an alarming increase in the more severe forms of

pregnancy toxæmia, as indicated in the following extracts from the Report²⁰ for 1940:

The abnormal conditions mentioned in last year's report have continued to prevail in the Colony during the year 1940, with an almost unimaginable state of overcrowding, malnutrition and distress among the lower classes from which most of our patients are drawn. There has been a grave increase in the amount of beri-beri, as will be seen from a perusal of the special table devoted to this disease. The table includes only the 155 cases of clinically obvious beri-beri, and among these cases there was a death-rate of 11 per cent, in spite of intensive treatment with vitamin B₁ preparations. There were many more cases of what might be termed "sub-clinical beri-beri" in patients living on the extreme border-line of the state to which poorness of nutrition was inevitably driving them, and there is no doubt that, if present conditions continue to prevail, we must expect a still further increase of avitaminosis B₁.

The classification of the toxæmias of pregnancy has been continued on the same basis described in last year's report, with satisfactory results. The frequent association of this condition with signs of avitaminosis B₁ during the year has again been noted, and biochemical studies have been continued . . . and will form the subject of a publication in the near future. The most alarming feature of the year's work was the occurrence of what might almost be described as an epidemic of eclampsia. There were 42 cases of this disease, as against 8 cases for the previous year. The severity of the disease was very marked and many of the worst cases were of the post-partum variety. There was a death-rate of 30 per cent among these patients, considerably more than half of which was due to complicating beri-beri and consequent heart-failure.

During the year 1941, for which only a manuscript report is available, conditions remained very much on the same level as in 1940, and the striking coincidence of a maintained increase in the total number of cases of beri-beri and a continued rise in the number of patients suffering from pregnancy toxæmia could not fail to strike the most casual observer. In Table I the inci-

dence of beri-beri complicating pregnancy during these three years is shown.

TABLE I.
Incidence of Beri-beri Complicating Pregnancy in Hong Kong, 1939-41

| Year | Cases of beri-beri | Total admissions | Incidence per 1,000 |
|--------|--------------------|------------------|---------------------|
| 1939 | 49 | 3,328 | 14.71 |
| 1940 | 155 | 4,738 | 32.71 |
| 1941 | 167 | 3,541 | 47.16 |
| Totals | 371 | 11,607 | 31.10 |

The incidence of the toxæmias of pregnancy during the same period is shown in Table II.

TABLE II
Incidence of the Various Forms of Pregnancy Toxaemia in Hong Kong, 1939-41

| Type of Toxaemia | 1939 | 1940 | 1941 | Total |
|-------------------------|-------|-------|--------|-------|
| Pre-eclampsia, Grade I | 112 | 128 | 221 | 461 |
| Pre-eclampsia, Grade II | 63 | 114 | 151 | 328 |
| Eclampsia | 8 | 42 | 29 | 79 |
| Nephritic toxæmia | 4 | 4 | 2 | 10 |
| Hypertensive disease | 13 | 4 | 13 | 30 |
| Totals | 200 | 292 | 416 | 908 |
| Incidence per thousand | 60.09 | 61.63 | 117.48 | 78.22 |

In studying Table II it is necessary to have some knowledge of the criteria upon which the classification of the toxæmia cases was based. After a careful study of the question, the classification shown in the appendix to this paper was adopted. It is based upon the recommendation of a Sub-committee appointed by the American Committee on Maternal Welfare in 1937 for the special study of the subject and agreed upon at the Annual Meeting of that body in June, 1940.²¹

It will be noticed that the first three conditions in the classification might be termed diseases dependent on, or peculiar to, pregnancy, whereas the last two belong to a group of diseases not peculiar to pregnancy. The classification was strictly

adhered to in compiling the patients' case records and many cases with transient high blood-pressure or albuminuria were consequently not included in the toxæmic groups. The emphasis placed on the findings of albuminuria on more than one occasion and on the persistence of a raised blood-pressure of 130 mm. Hg. or higher for 2 days or longer ensures that only patients with genuine toxæmias were included, and also explains why a patient classified as suffering from pre-eclampsia, Grade I (mild), might be recorded as having a single maximal blood-pressure reading of over 150 mm. Hg.

In investigating the relation between avitaminosis B₁ and pregnancy toxæmia, extensive biochemical studies were conducted on all likely cases in addition to the usual clinical investigation. These studies included estimation of the carbon dioxide combining power, non-protein nitrogen, urea, uric acid, plasma proteins, chlorides, and pyruvic acid contents of the blood as well as parallel quantitative determinations of the vitamin B₁ content of both blood and urine. These observations were carried out on considerably more than 200 cases, but unfortunately, with the exception of the results of pyruvic acid determinations on 207 patients, the whole of the rest of the biochemical data was destroyed by enemy action in Hong Kong (it was actually in the process of being assembled for publication when the war broke out in December 1941). The data presented in this paper are therefore very largely based on the brief case summaries which had been prepared and which it has been found possible to salvage.

In further studying the case histories of patients included in Tables I and II it was found that 252 of them showed evidence that they were suffering from a combination of beri-beri and pregnancy toxæmia. In other words, of the 371 cases of beri-beri with which this paper is concerned, ap-

proximately 70 per cent were complicated by one or other of the forms of pregnancy toxaemia. Conversely, 28 per cent of the 908 cases of pregnancy toxaemia showed fully developed manifestations of beri-beri.

The combined incidence of beri-beri and pregnancy toxaemia is shown in Table III.

CLINICAL FINDINGS.

The following summary of the clinical findings in the 371 cases which form the subject of this paper may be of interest:

(1) *Age and parity.* The group consisted of 125 primiparae (33.4 per cent), with

TABLE III.
Incidence of Pregnancy Toxaemia in 371 Cases of Beri-beri Complicating Pregnancy

| Clinical condition | 1939 | 1940 | 1941 | Totals |
|--|------|------|------|--------|
| Beri-beri with normal pregnancy . . . | 32 | 47 | 40 | 119 |
| Beri-beri with pre-eclampsia, Grade I | 2 | 38 | 52 | 92 |
| Beri-beri with pre-eclampsia, Grade II | 12 | 52 | 58 | 122 |
| Beri-beri with eclampsia . . . | 2 | 18 | 16 | 36 |
| Beri-beri with nephritic toxaemia ... | 1 | — | — | 1 |
| Beri-beri with hypertensive disease | — | — | 1 | 1 |
| Totals .. | 49 | 155 | 167 | 371 |

The findings shown in this table are very significant, and they are shown in graphic form in Fig. 1, which brings out clearly not only the increase found in the total number of cases of beri-beri during the 3 years, but the relative increase in the incidence of complicating pregnancy toxaemia during the latter 2 years. It might be argued that the increase is apparent rather than real and that the true state of affairs can only be appreciated by considering the facts in relation to the number of cases admitted to the wards. Fig. 2 has therefore been prepared showing the incidence of pregnancy toxaemia, beri-beri and the combination of both conditions per 1,000 cases admitted to the obstetrical wards. Since the total number of admissions for the year 1941 was less than that for 1940, this method of representing the position shows even more clearly the striking bond which appears to exist between an increase in the beri-beri rate on the one hand and an increase in the toxaemia rate on the other, a bond which is still further strengthened by the co-existence of the two conditions in a significant number of cases.

an average age of 23.6 years and 246 multiparae (66.6 per cent), with an average age of 29.9 years. This distribution is almost exactly similar to that found in the total number of cases admitted, so that no special association was noted between the incidence of beri-beri and the age or parity of the patient. (This contrasts with the 908 cases of pregnancy toxaemia of whom over 66 per cent were primiparae.)

(2) *Twin pregnancy* was found in 15 out of the 371 cases of beri-beri, an incidence of 1 in 24.7. This compared with an incidence of 1 in 26.7 for the 908 cases of pregnancy toxaemia and a general incidence of 1 in 105.7 for all cases delivered during the same period.

(3) *Oedema.* Oedema was present in all but 13 of the patients, an incidence of over 96 per cent. The duration of the oedema ranged from a few days to 6 months, but averaged 44.77 days in the 371 cases. In many instances the oedema was the most conspicuous feature. It generally commenced in the feet and legs and extended upwards over the body, being usually very noticeable in the abdominal wall. Ascites,

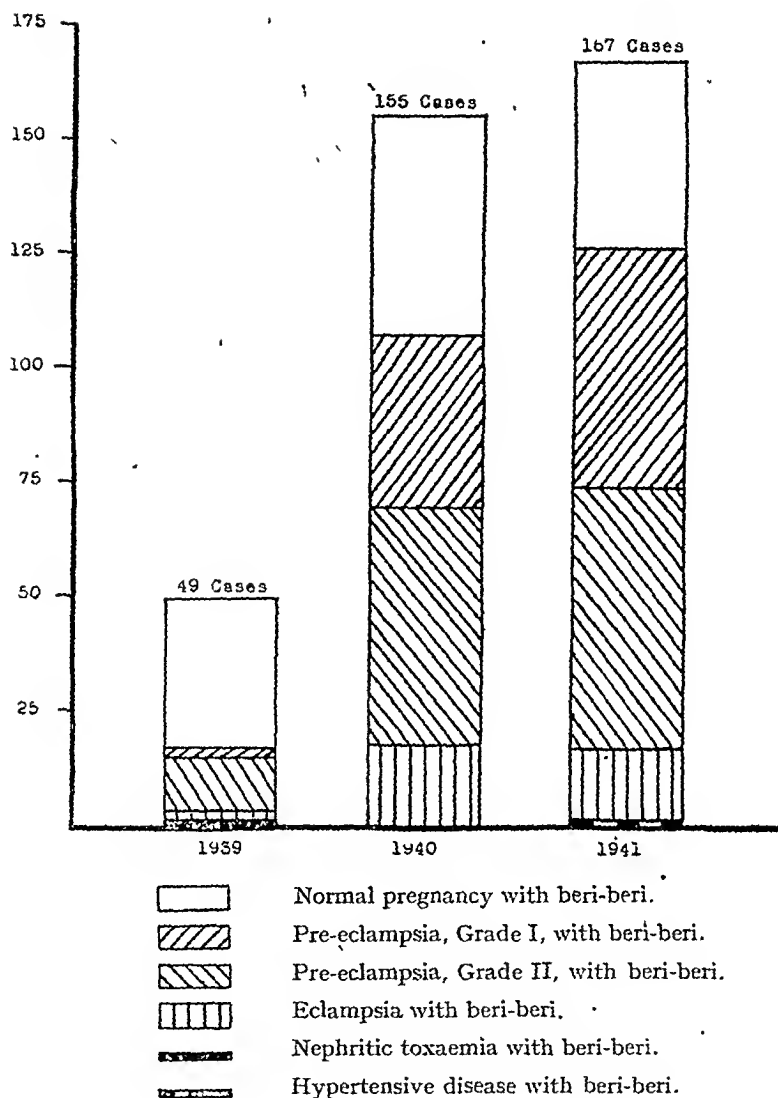


FIG. 1.

DISTRIBUTION OF 371 CASES OF BERI-BERI COMPLICATING PREGNANCY.
(Hong Kong, 1939 to 1941)

pulmonary oedema, hydro-thorax and hydro-pericardium occasionally developed. The latter was usually a prominent feature in the cases that came to post-mortem. It was generally the "wet" form of beri-beri, therefore, which was encountered in Hong Kong. In this connexion it is interesting to

note that McCarrison believes that wet beri-beri occurs in partial and prolonged deficiency of vitamin B₁, and that the dry form occurs in complete absence of vitamin B₁.

(4) *Nervous changes.* The condition of the reflexes, the presence or absence of

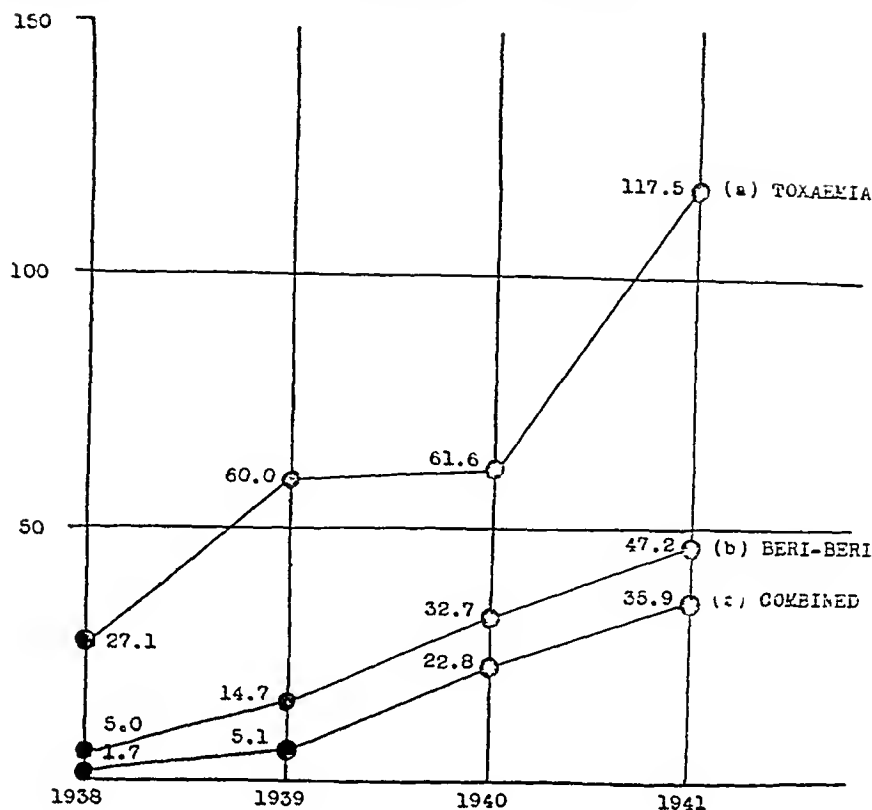


FIG. 2.

Showing rising annual incidence per thousand admissions of
 (a) Pregnancy toxemia; (b) Beri-beri; (c) Combined toxemia and beri-beri
 (Hong Kong, 1938 to 1941)

anaesthesia, hyperaesthesia and muscular weakness or wasting was investigated in all cases.

The knee jerks and ankle jerks were found in rare early cases to be exaggerated, later to become weak and sluggish and finally to be completely abolished. The knee jerks were recorded as being exaggerated in 3 patients, present in 33, sluggish in 6 and entirely absent in 323 (there was no record in 6 cases). Areas of cutaneous anaesthesia and numbness were found in 65 cases. Hyperaesthesia, particularly sensitiveness to deep pressure over the calf muscles, was found in 149 cases. Muscle changes varied from slight wasting to

marked atrophy, and, in the worst cases, an inability to walk. Such changes were present in 212 cases. There was no noticeable change in 110 cases, and records were not available in 49 cases. The muscles of the foot and calf were those usually affected, but later the extensor and flexor muscles of the thigh were involved, by which time foot-drop was often present. In more severe cases the arm muscles and the muscles of the trunk and even the diaphragm were sometimes affected.

(5) *Cardio-vascular changes* were those most to be feared in these cases. During pregnancy, and more especially as the time for the onset of labour approached, patients

of treatment remained substantially the same. The association of beri-beri with eclampsia was noticed in 36 out of the 79 cases. Fourteen of these cases died, giving a mortality-rate of 38.8 per cent for eclampsia complicating beri-beri as against 11.6

disease, etc. There is usually an interval between the time when the patient begins to suffer from a depletion of vitamin B₁, and the appearance of the symptoms of beri-beri. During this interval, which may last for many weeks or months, the patient is

TABLE VII.
Mortality Rates in 908 Cases of Pregnancy Toxaemia.

| Clinical condition | Number of cases | Maternal deaths | | Infant deaths* | |
|----------------------------|-----------------|-----------------|----------|----------------|----------|
| | | Number | Per cent | S.B. & N.D. | Per cent |
| Pre-eclampsia, Grade I . | 461 | 4 | 0.9 | 39 | 8.2 |
| Pre-eclampsia, Grade II .. | 328 | 9 | 2.7 | 43 | 12.4 |
| Eclampsia | 79 | 19 | 24.1 | 26 | 31.7 |
| Nephritic toxaemia . | 10 | 1 | 10.0 | 3 | 30.0 |
| Hypertensive disease .. | 30 | — | — | 2 | 6.6 |
| Totals: | 908 | 33 | 3.6 | 113 | 12.0 |

* S.B.—Stillbirth, N.D.—Neonatal death.
Stillbirth figures include 4 infants who died undelivered.
There were 34 twin deliveries.

per cent for the 43 cases of eclampsia without manifest signs of beri-beri, a figure much more in accord with previous experience.

DISCUSSION.

A deficiency of vitamin B₁ may arise from:

- a deficiency in the diet,
- a failure of absorption,
- a deficient storage capacity,
- a failure of utilization,
- an increased requirement.

Human beings are unable to synthesize vitamin B₁, nor can they store it in the body tissues to any extent: they are therefore very liable to develop beri-beri in the presence of predisposing factors. Such factors include poverty, with consequent dietary deficiency, pregnancy, lactation and any other circumstance which calls for an increase in the metabolic rate, such as increased physical exertion, hyperthyroidism, febrile

symptom free, but exists on an abnormally low thiamine intake. This intervening period might be called the stage of sub-clinical beri-beri. The appearance of any unusual call on the body reserves, such as increased exertion, pregnancy or an acute illness, might be sufficient to precipitate the patient into a condition of fully developed beri-beri.

In Hong Kong, during the period under review, the train of circumstances could be very clearly traced. Beri-beri has always been endemic in South China, and there is evidence that the condition was recognized by the Chinese²⁵ as early as 2697 B.C. In Hong Kong the disease had always been present among the lower classes and among those whose diet consisted largely of polished rice. During the years under review the general medical service of the Colony encountered a very marked rise in the incidence of beri-beri and the gravity of the situation was repeatedly emphasized in the Annual Reports of the Director of Medi-

cal Services.²⁶ In actual fact the total deaths from beri-beri in the Colony rose from 3,189 in 1939 to 7,229 in 1940. As pointed out in these reports, the increase in beri-beri was a real, and not an apparent one, brought about by an unprecedented influx of refugees from war areas with consequent poverty and overcrowding, all factors which helped to render the conditions ideal for the development of beri-beri. A further factor was the extreme unwillingness of the people to eat anything but polished rice, although great efforts were made to popularize the eating of unpolished or "red" rice. The increase in the amount of beri-beri seen among obstetrical patients was, therefore, only the natural reflection of a generally prevailing condition.

In the 371 cases reported in this paper, manifest signs of beri-beri were encountered. There were, however, two additional groups of cases which came into prominence during the same period, and which appeared in some way to have a relation with the beri-beri cases. On the one hand there was a large group of 676 cases with simple oedema uncomplicated by any other signs of beri-beri or of pregnancy toxaemia. It was tempting to place all of these cases in the beri-beri group, but in the absence of complete proof as to the origin of the oedema the authors preferred to place these cases in a separate class. There is little doubt in the minds of the writers, however, that the oedema was of nutritional origin, and that these 676 cases were examples of sub-clinical beri-beri. On the other hand there was a still larger group of 908 patients suffering from pregnancy toxaemia in one form or another. This gives a general toxaemia-rate of 7.82 per cent for the three years 1939, 1940 and 1941, as compared with the much lower rate of 3.45 per cent for the preceding three years 1936, 1937 and 1938. A striking increase in the toxaemia-rate running *pari-passu* with the figures of

an unprecedented outbreak of beri-beri would seem to the writers to be more than a mere coincidence.

Perhaps the most interesting feature of the whole series of cases, however, was the fact that 70 per cent of the patients with beri-beri showed co-existing evidence of pregnancy toxaemia. This fact, together with the tendency, just noted, to a parallel increase in the figures for both diseases, would seem to point to the conclusion that the association between nutritional oedema, beri-beri and pregnancy toxaemia is by no means a fortuitous occurrence. The combination of the manifestations of beri-beri (such as oedema, polyneuritis, cardiovascular symptoms and a high pyruvic acid content of the blood) with the usual evidences of pregnancy toxaemia (such as high blood-pressure, albuminuria, increased uric acid content of the blood and, in some cases, typical eclamptic convulsions) provided a clinical picture at once interesting and complicated. Vitamin B₁ therapy was naturally used in treating patients who showed clear signs of deficiency. In treating these patients it became more and more manifest that an almost uniform improvement resulted in the great majority of all cases of beri-beri and toxaemia, whether simple or combined. It finally became customary to treat all these patients with thiamine, in addition to the usual dietary, eliminative, sedative and other methods of treatment appropriate to the clinical condition. The conviction grew in the minds of the writers that a causal relation exists between a relative or actual deficiency of vitamin B₁ on the one hand, and the occurrence of pregnancy toxaemia on the other. They feel that their view is supported by the following facts:

(a) There was an almost parallel increase in the incidence of beri-beri and pregnancy toxaemia in Hong Kong during the years 1939, 1940 and 1941. During these years

the toxæmia-rate rose to 7.82 per cent as compared with 3.45 per cent in the preceding 3 years.

(b) There was a greatly increased incidence of twins in both groups of cases (1 in 24.7 for the beri-beri group, and 1 in 26.7 for the toxæmia group as compared with a general incidence of 1 in 105.7 for all deliveries).

(c) In 70 per cent of the cases suffering from beri-beri pregnancy toxæmia was present in one of its forms as a complicating factor. In the remaining 30 per cent of cases the blood-pressure was generally higher than that usually seen in beri-beri.

(d) There was a phenomenal increase in the incidence of eclampsia during these years, 45.5 per cent of the cases being complicated by frank beri-beri. The eclampsia mortality-rate rose from 12.1 per cent in normal times to 24.1 per cent during the period under review, and in the beri-beri group the mortality was over three times as high as in the uncomplicated group.

(e) There was an even greater increase in the incidence of the severe type of pre-eclampsia during the same period.

(f) Blood pyruvic acid determinations showed the high levels typical of vitamin B₁ deficiency in a large proportion of the cases of toxæmia.

(g) The lost studies of the writers on the quantitative vitamin B₁ content of the blood and urine added further support to the evidence.

(h) The therapeutic effect of the administration of vitamin B₁ was often as marked in cases of severe pregnancy toxæmia as in typical cases of beri-beri. In many patients suffering from severe pre-eclampsia it was felt that the onset of convulsions was averted by vigorous treatment with vitamin B₁ in addition to the usual methods adopted in such cases.

Such a view is supported by the findings of various workers whose writings have

been quoted earlier in this paper. Nevertheless, some authors have argued that the use of thiamine in pregnancy toxæmia is not only useless but possibly even harmful. This is difficult to understand in view of the established fact that the need for vitamin B₁ is increased about three times during pregnancy and lactation, and that in human beings there is no recognized overdosage of vitamin B₁. In dogs the lethal dose of vitamin B₁ has been stated to be 350 mg. per kilogram. It has been shown that a human being can tolerate a dosage of 500 mg. daily for as long as a month with no adverse signs. This dosage is far in excess of anything likely to be used clinically, and the writers have never noticed any adverse effects from the use of dosages up to 180 mg. per day in severe cases of cardiac beri-beri with complicating toxæmia.

The nature of the relation between vitamin B₁ deficiency and the toxæmias of pregnancy is more difficult to discuss, and at the present time the authors are not prepared to offer an opinion as to whether hypovitaminosis B₁ merely predisposes to the development of pregnancy toxæmia or whether the deficiency is the actual causal factor. They incline towards the latter view, but the proof which they had hoped to produce was destroyed when almost within their grasp. A discussion as to the nature of the origin of oedema is beyond the scope of this paper, but a theory which has appealed to the writers is that vitamin B₁ is essential to the proper functioning and well-being of the endothelium of the blood-vessels as well as to the peripheral nerve fibres. In the event of a deficiency of vitamin B₁, degeneration of the endothelial cells and nerve fibres occurs with the consequent appearance of oedema and evidences of polyneuritis; if the vagus nerve is affected the heart will also show signs of disturbance, and one or more of the well-known clinical forms of beri-beri will result. In the event

of pregnancy occurring an increased strain is imposed on the maternal organism. In an effort to secure the proper nutrition of the foetus the blood-pressure rises and overcomes the barriers imposed by oedema. In this way the manifestations of pre-eclampsia may arise and, in certain cases, eclampsia itself may occur. A recent communication by Rosenbaum and Maltby²⁷ suggests that eclampsia is likely to occur in patients who have evidence of a primary cerebral dysrhythmia. In 65 per cent of 20 cases with eclampsia they found electroencephalograms indicative of cerebral dysrhythmia. They suggest that such a condition may be present in patients who develop eclampsia and that an associated toxæmia may act as the trigger mechanism which exaggerates the inherent dysrhythmia to the extent that convulsions appear. In the event of such an hypothesis proving true it would be easy to understand how eclampsia could readily occur in severe cases of beri-beri complicated by pregnancy toxæmia, and it would, to some extent, explain the unduly high incidence of eclampsia in the present series of cases.

SUMMARY AND CONCLUSIONS.

1. There was a striking increase in the incidence of beri-beri in Hong Kong during the years 1939, 1940 and 1941. This was a true increase and was seen in general medical and surgical cases as well as in obstetrical cases.

2. There was an almost parallel increase in the incidence of pregnancy toxæmia during the same period, especially in cases of eclampsia and of severe pre-eclampsia. This also was a true increase, the toxæmia-rate rising from 3.45 per cent during the preceding 3 years to 7.82 per cent during the 3 years under review.

3. Some correlation between these figures

is inescapable, and it was found that, out of 371 cases of beri-beri complicating pregnancy during this period, no fewer than 252 cases were further complicated by pregnancy toxæmia.

4. The diagnosis of beri-beri and pregnancy toxæmia was supported by both clinical and laboratory findings. Significantly high readings of the pyruvic acid content of the blood were obtained in the great majority of cases.

5. In cases suffering from toxæmia with complicating manifestations of beri-beri, the prognosis was considerably more grave than in cases of toxæmia without frank signs of beri-beri. This was particularly seen in the eclampsia cases, in which a mortality-rate of 38.8 per cent was found in 36 cases complicated by beri-beri, as opposed to 11.6 per cent in 43 uncomplicated cases.

6. It is suggested that the primary factor responsible for the heavy increase in pregnancy toxæmia during the years under review was vitamin B₁ deficiency. Arguments are advanced in support of the view that a causal relation exists between a deficiency of vitamin B₁ and the occurrence of pregnancy toxæmia.

7. Prophylaxis and/or active treatment by the exhibition of adequate amounts of vitamin B₁, whether in the form of a vitamin-rich diet or as thiamine medication, is suggested as perhaps the most important single measure in dealing with pregnancy toxæmia in any of its forms.

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APPENDIX.

CRITERIA FOR THE CLASSIFICATION OF THE TOXAEMIAS OF THE LATTER HALF OF PREGNANCY.

(1) *Pre-eclampsia, Grade I (Mild).*

The appearance during the latter half of pregnancy and disappearance by the 6th week postpartum of two or more of the following:

- (a) Systolic blood-pressure of 130 or higher for 2 days or longer.
- (b) Albuminuria on more than one occasion.
- (c) Oedema of the legs and ankles which has no other obvious cause.

(2) *Pre-eclampsia, Grade II (Severe).*

The appearance during the latter half of pregnancy and disappearance by the 6th week postpartum of the signs noted above with the addition of one or more of the following:

- (a) Systolic blood-pressure over 150 for 2 days or longer.
- (b) Albuminuria with granular casts or albumin in excess of 2 gm. per litre.
- (c) Excessive oedema.
- (d) Any of the danger signals of impending eclampsia such as headache, tinnitus, visual disturbance, epigastric pain, vomiting, jaundice, suppression of urine, etc.

(3) *Eclampsia.*

- (a) *Convulsive type*: The appearance of typical convulsions in a case showing some or all of the signs noted above.
- (b) *Non-convulsive type*: The development of coma in a patient showing some or all of the signs noted above (particularly jaundice) with postmortem findings typical of eclampsia.

(4) Nephritic Toxaemia.

The presence before pregnancy or appearance before the 30th week of pregnancy and/or the persistence for longer than 6 weeks post-partum of 2 or more of the following evidences of renal disease:

- (a) Hypertension.
- (b) Oedema.
- (c) Albuminuria.
- (d) Albuminuric retinitis.
- (e) Impaired renal function.
- (f) Nitrogen retention in the blood.

Renal disease may be classified as:

- (a) Glomerulo-nephritis.
- (b) Nephro-sclerosis.
- (c) Nephrosis.

(5) Hypertensive Disease.

- (a) *Benign or essential hypertension.* A systolic blood-pressure persistently above 130, either present before pregnancy or appearing during pregnancy, and persisting longer than 6 weeks post-partum. There may be slight albuminuria and oedema as term approaches, but the height of the blood-pressure is out of proportion to these signs. The renal function is normal and the retina is normal or may show some narrowing of the vessels.
- (b) *Malignant hypertension.* Typical changes take place in the retina and later there is impairment of the cardiac and renal functions.

Studies in X-ray Pelvimetry

An Evaluation of Pelvic Radiography, with a Plea for Simplicity

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INTRODUCTION.

THE purpose of the present paper is mainly to report a study on 60 dry pelvises in which Nicholson's formula¹ for finding the areas of the pelvic brim and outlet is put to the test. But an attempt has also been made to bring X-ray pelvimetry closer to its true level of value; and technique which corresponds more faithfully with its possibilities is recommended. Certain fundamental observations are set out which, if not new, have been verified experimentally: there is too much uncertainty about these facts, and it is necessary to avoid the confusion that is apparent in writing and in discussion alike.

If we are of the opinion that operative obstetrics has advanced, it must still be admitted that there is no method of predicting with certainty whether a given pelvis will cause serious obstruction to the foetal head or not. If one held the bony pelvis in one's hand for inspection and were able to make direct measurements, a very wise assessment of the adequacy of such a pelvis could be worked out; but with a number of specimens this prognosis is conditional on so many factors that it will be obvious to the critical pupil that there is no absolute means of knowing whether a head will pass through the girdle or not. When this problem is applied to the living subject, there is the added difficulty that the bony pelvis can neither be seen nor readily measured.

X-ray pictures of its different aspects will tell something of the bony shape, and the application of certain principles will even give some measurements.

The failure of radiology to solve single-handed the problem of dystocia due to disproportion led to disappointment, and the opinion that only clinical experience based in digital pelvic examination was of value. The latter idea is defeatist, for the clinician of sound experience knows not only his limitations but also his inability to guide members of that large group on which women are dependent for their delivery. In a word, we are still unable to reduce labour to mathematics. Even brilliant clinical ability aided by pelvic radiology falls short of this objective. This notwithstanding, it may well be possible to simplify our radiological requirements for each case sufficiently to give guidance to the average accoucheur. It would be contemptible to deprive him of the help of an accessory method by making it too complicated; as if to imitate Nature, who has put the basic secrets of parturition just beyond the reach of the wisest and most experienced obstetricians.

It may be asked whether anything reliable may be gained from an X-ray study of the obstetric pelvis. It has to be admitted that, in order to answer different questions about a pelvis, several radiographic views may be necessary and that, for the pur-

pose of measurement, various modifications may be required. But for general use it is necessary to devise a method which is both simple and of an accuracy which is clearly known. With this in mind, we must make a decision about the salient features of the pelvis which will not only contribute towards its classification but also give its capacity. Our first object, then, is clear. And as the skiagram increases knowledge regarding the mechanism of labour, so more will inevitably be demanded of it.

PART I.

Nicholson¹ suggested that the four functions of the pelvis which are of value for obstetrics are: the pelvic index and area of the brim, the area of the outlet, and the subpubic angle. It is proposed that two more should be considered, viz., the depth of the pelvic basin and the height of the symphysis pubis. But we wish particularly to avoid complicating the method of X-ray pelvimetry. Therefore, although on academic grounds we believe that the 6 features of the pelvis mentioned above are the ones essential to prognosis, for general purposes all that is required is a knowledge of the areas of the inlet and outlet, and the pelvic brim index. The height of the symphysis pubis can readily be measured with a pelvimeter, and the capacity of the pubic arch assessed by palpation.

As early as the middle of the 18th century Roederer² "likened the superior strait to an ellipse" (W. Williams); and in von Stein's⁴ classification three pelvic types were designated: round, longitudinal-elliptical, and transversely-elliptical. But it was Nicholson¹ who made use of the fact that the shape of the pelvic brim closely resembles an ellipse of which the axes are the conjugate and greatest transverse diameters. Similarly, at the outlet the area of the plane of least pelvic diameters can be

calculated from two axes, viz., the inter-spinous and pubosacral diameters. This formula was adopted in studying their series of pelves by both Nicholson¹ and by Ince and Young.³ So significant is Nicholson's suggestion that it was decided to test the accuracy of his formula on skeletal material.

EXPERIMENTAL.

Diophtographic tracings were made of the brim of the pelvis and outlet, and areas were obtained both by calculation and by means of a planimeter. The latter area would be the true area, and in this study a maximal accuracy to the nearest $\frac{1}{16}$ th of a square centimetre was attained.

The area of the pelvic brim. Sixty female pelves were used, 52 of which were from the Bantu collection described elsewhere and 8 of mixed "coloured" race. In each case the area calculated by Nicholson's formula was smaller than the true or planimeter area. The percentage error ranged from -1.5 per cent to -20.3 per cent. As the greater figure occurred in an example of spondylolisthesis where the promontory of the sacrum projected unduly into the plane of the brim, thus interfering with its shape as an ellipse, it may be stated that the next greatest error amounted to -13.1 per cent. The average error was -8.5 per cent, but 19 out of 60 observations showed an error of over 10 per cent.

The main source of this large error was found to be the promontory. Thus, if the sweep of the brim outline was continued with a disregard for the sacral promontory, a complete flattened circle was obtained. A large sacral promontory which projects far across the pelvic basin unduly shortens the conjugate and reduces the pelvic index. Reliance on the brim width of this diameter, which still remains in obstetrics, can make a pelvic appearance of normality whereas the area of the pelvic brim is

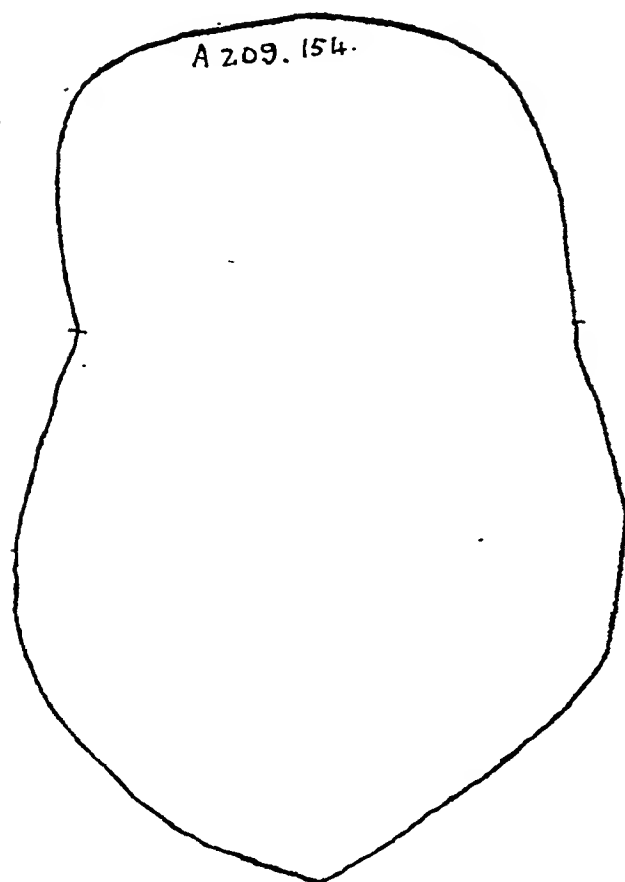
counting this encroachment of the promontory, may be larger by as much as 10.0 sq. cm. or more. Even if the conjugate is shortened sufficiently to obstruct passage of the foetal head, the transverse diameter of the brim may be absolutely increased and allow easy engagement of the head. The pelvic cavity below this plane would then, all things being equal, accommodate the head with ease. It may be demonstrated by anyone too, that a skiagram of the pelvis with the brim horizontal or nearly so, does not show the anterior border of the promontory. A piece of lead wire placed along this edge in a specimen of the pelvis lies well forward of any shadow of bone that can be identified on the film. It is necessary that both these facts should be recognized, and the matter may be stated thus: that the sacral promontory should be disregarded for the reasons mentioned, and because of the fact that in the mechanism of engagement of the foetal head it is not necessarily an obstruction; and that in any case the whole promontory is not outlined in the so-called A.P. X-ray views.

The diophtographic tracings were, therefore, enlarged by completing the posterior portion of the pelvic brim curve and so removing the encroachment of the promontory (Fig. 3). This is very readily done on the radiograph where a portion only of the projecting bone is seen. The new conjugate diameter would then be longer, and the calculated area would be correspondingly greater than before. The planimeter area would also be increased, most frequently by about 5.0 sq. cm. but occasionally by more than 10.0 sq. cm. With this modification it was found that the formula and planimeter areas corresponded closely. In 60 pelvises the average area of this complete ellipse was 116.6 sq. cm. by the planimeter and 116.3 sq. cm. by calculation. The percentage error was both positive and negative, and varied from

-4.9 to +9.6. In 11 cases the error was above 3.5 per cent, and in only 2 of these above 5.0 per cent (+5.2 per cent and +9.6 per cent). Fig. 4 shows a comparison of the error obtained by Nicholson's formula and the modification here suggested. The blackened blocks are very much smaller than the large plain ones, both representing the mean error of calculation for different ranges of area obtained by the planimeter. The calculation of the modified area of the brim can be said to be well within an error limit of 5.0 per cent.

Even so high an error as 5 per cent may be avoided. It must be remembered that the shape of the brim is considered as an ellipse, and where this shape departs grossly from this flattened circle there is a liability to error. In studying the brim tracings the observation was made that either asymmetry or an "angular" suprapubic angle led to the highest error. In 8 of the 11 areas in which the error was above 3.5 per cent the two oblique diameters of the brim differed by 0.5 cm. or more, the range being 0.5 cm. to 0.9 cm. Of the other 3 pelvic brims, 2 had equal oblique diameters, and 1 showed a difference of 0.2 cm.; in 2 of these there was marked asymmetry of the fore pelvis, and in one where the error was +9.6 per cent the brim was beak-shaped. Now it will be obvious that where the anterior half of the brim is nearly triangular, the actual area will be less than that of an ellipse with axes equal to those of the beak-shaped brim.

An attempt was made to reduce these 11 brim tracings to two half-ellipses, or to take the posterior portion of the brim as a half ellipse and the anterior portion as a triangle. But the sum of the calculated areas of these portions did not give an accurate final result. It is suggested, therefore, that where there is asymmetry of a brim as seen on the radiograph, or an undue narrowing to an angular shape at the symphysis



| | |
|-----------|--------------|
| I.I.S. | 6.3 cm. |
| A.P.O. | 11.1 cm. |
| Max. T.O. | 7.8 cm. |
| P. | 68.1 sq. cm. |
| F. | 54.9 sq. cm. |
| Ell. | 68.0 sq. cm. |

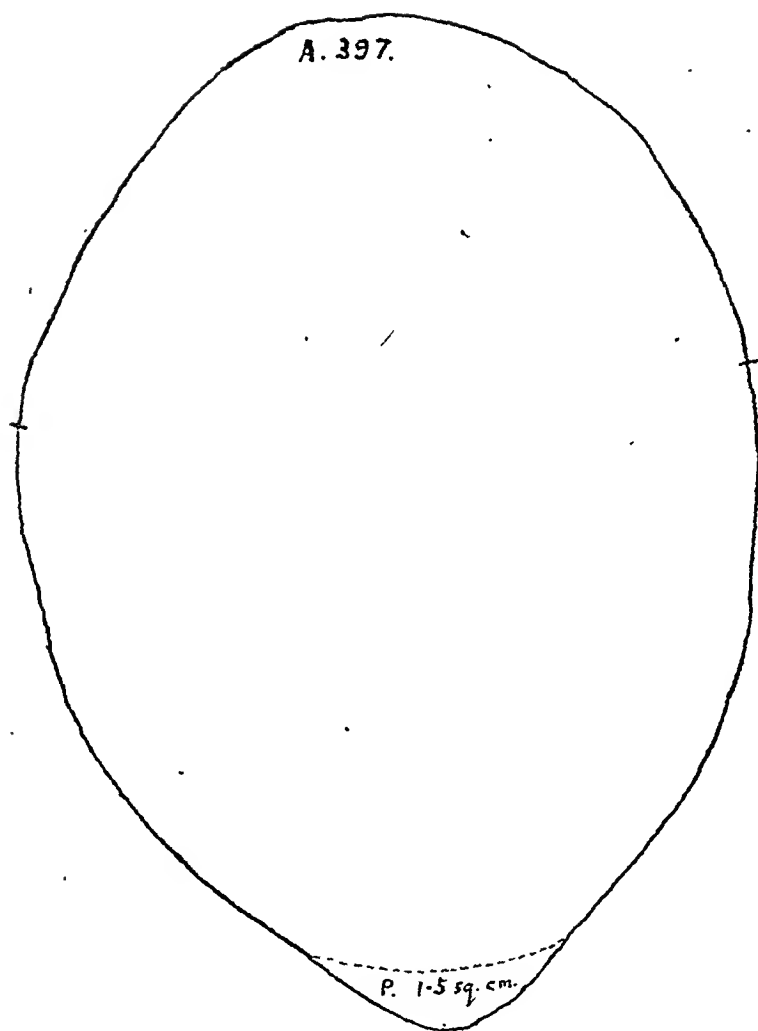
Error 13.2 sq. cm., or - 19.4 per cent.

Ellipse area = true area.

FIG. 1

Dioptographic tracing of plane of least pelvic diameter (A.209). The exaggerated size of the ischial spines reduces the interspinous diameter too much to allow it to operate as an axis in the calculation of this area as an ellipse.

| | | |
|-----------|---|---|
| I.I.S. | = | inter-ischial spine diameter. |
| A.P.O. | = | pubo-sacral diameter. |
| Max. T.O. | = | maximal transverse diameter of tracing. |
| P. | = | planimeter area |
| F. | = | area calculated from I.I.S. and A.P.O. (Noble's) |
| Ell. | = | area calculated from Max. T.O. and A.P.O. (ellipse) |



| | |
|-----------|--------------|
| I.I.S. | 9.6 cm. |
| A.P.O. | 13.0 cm. |
| Max. T.O. | 9.6 cm. |
| P. | 94.1 sq. cm. |
| F. | 98.1 sq. cm. |
| Ell. | 98.1 sq. cm. |

Error 4.0 sq. cm. or 4.25 per cent.

Ellipse area = F. area.

FIG. 2.

Dioptrographic tracing of plane of least pelvic diameter, showing the effect of an angular anterior pole on the calculated area (A.397).

Note on A.397.—This outlet shape is very close to the perfect ellipse. The discrepancy, however slight, in the result of the formula is probably due to the angle which the outline gives when the under-surface of the symphysis is approached. This angular shape at that pole of the ellipse is unavoidable. If this "angle" is eliminated, it will be observed that the formula gives a result very close to the true area given by the planimeter.

With A.P.O. 12.3, F. = 92.77 sq. cm.

For this area P. = $(94.1 - 1.5)$ sq. cm.

= 92.60 sq. cm.

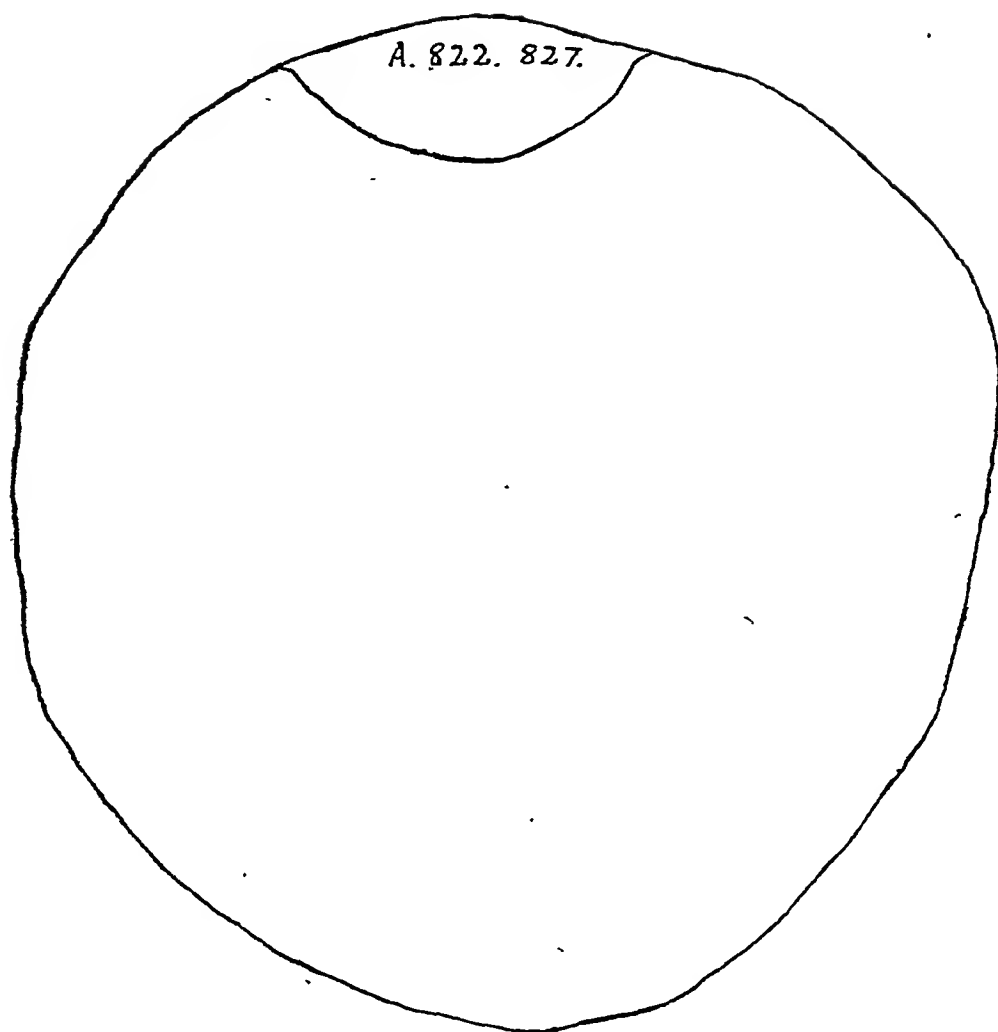


FIG. 3.

Dioptographic tracing of pelvic brim (A.822. 827).

Area of plane of brim by planimeter = 123.2 sq. cm.

Area of plane of brim by calculation = 111.9 sq. cm.

Error = - 9.2 per cent.

Planimeter area of plane of brim eliminating promontory = 128.1 sq. cm.

Calculated area of plane of brim eliminating promontory = 128.6 sq. cm.

Error = + 0.4 per cent.

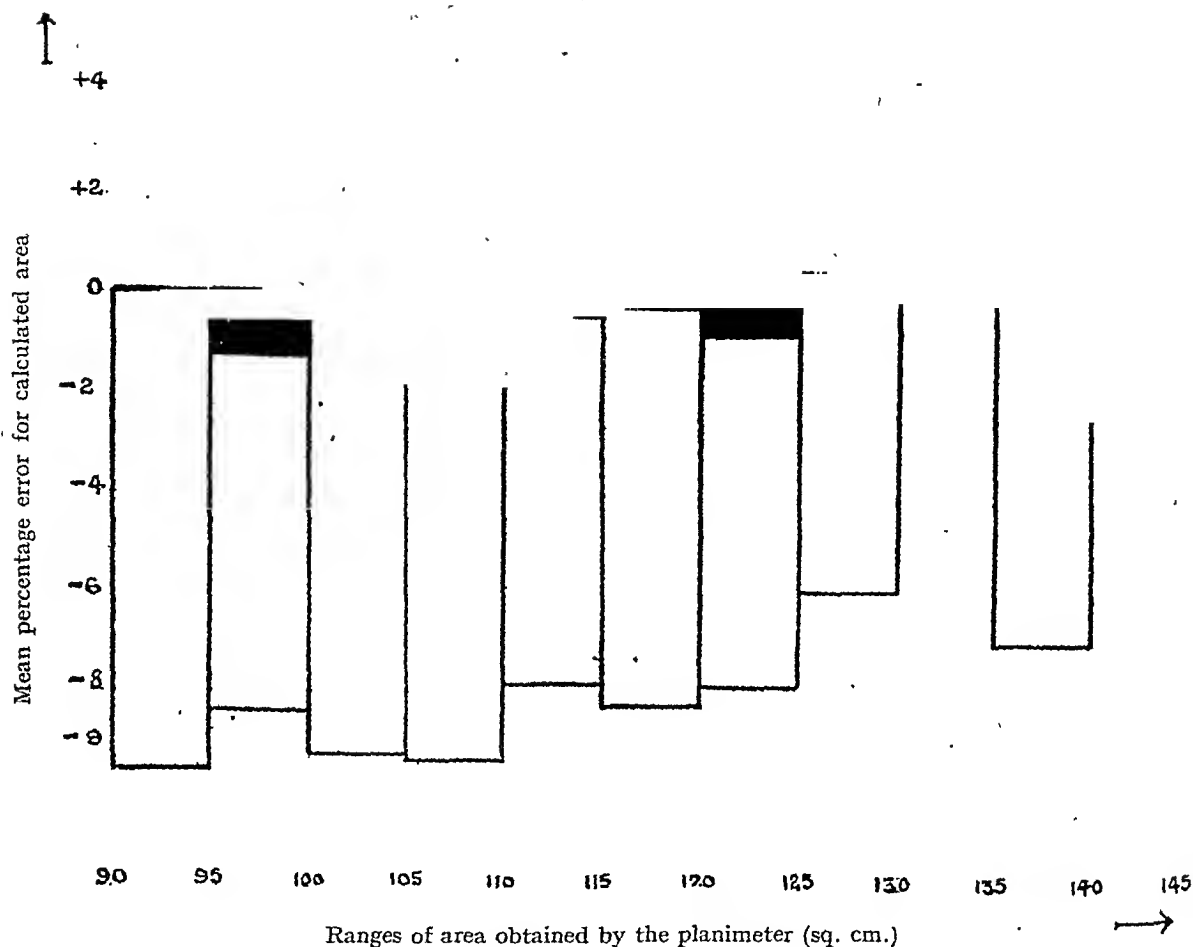


FIG. 4.

Area of the pelvic brim—a comparison of the accuracy of two methods of calculation.

The open blocks represent the mean error for areas obtained by Nicholson's formula, the solid blocks the smaller error for areas obtained by modification suggested in this paper.

Ranges of 5 sq. cm. of planimeter areas have been taken, and the two mean percentage errors found for the corresponding areas obtained on calculation by the two methods respectively.

pubis, our method of calculation should be suspect. In these cases the area should be determined by making a tracing from the X-ray film and applying to it either graph paper or a planimeter. Use of the planimeter is much more rapid and accurate, but if the instrument is not available there should be no difficulty about the use of squared paper.

It was found that the shape of a brim might be asymmetrical and yet give an accurate area by calculation. Careful examination in such a case might show it to resemble an ellipse lying obliquely, or it may be a matter of luck that the axes were of a length to give an accurate result. In view of these findings, it may be stated that only with grossly abnormal brim shapes is there the likelihood of an error exceeding 5.0 per cent. This figure of 5 per cent means, on the average, an area of about 5.0 sq. cm. which is too small to influence our present knowledge of the effects of the pelvis on labour. When accuracy for academic purposes is required, all asymmetrical brims should have the area determined directly, not by calculation; and this procedure should be adopted by all other workers when in doubt.

The area of the plane of the outlet. This success with the brim areas was not attained when the outlet was studied. Dioptraphic tracings were made after numerous methods for this purpose had been tried. In some cases the outlet plane (plane of least pelvic diameters) could be seen entirely from above only, in others mainly from below. It was found that inaccuracy resulted from viewing an outlet partly from above and partly from below. Stiffened white cord was used in a suitable length and fixed with small pieces of plasticine to run from the lower end of the sacrum in a curve towards the ischial spines and thence to the lower end of the symphysis pubis. From the ischial spines forward the cord

would hug the lateral wall of the pelvis at the correct level. Viewed from below only, the outlet could in most cases be traced with sufficient accuracy, even though the cord disappeared for a part of the distance anterolaterally.

The ellipses obtained at the outlet were much more perfect than those at the level of the brim. Nevertheless, the axes of the brim were true, being the longest diameters of the brim. At the outlet the axes used were the pubosacral and interspinous diameters, the latter of which is not a true axis, being posterior to the transverse axis which is usually longer than the interspinous diameter. It will be understood, therefore, that, if the interspinous diameter lies close to the sacrum and the ischial spines are large and project unduly towards the midline, this diameter will be considerably shorter than the true transverse axis of our outlet ellipse. The result would be a reduction of the calculated area relative to the true area. This feature may be counteracted by a narrowing of the anterior portion of the ellipse which may tend towards angularity; and for this reason the calculated area is often more accurate than one would expect.

Twenty pelves were studied: the true area was obtained with a planimeter, an area of the ellipse calculated with pubosacral and interspinous diameters as axes, and a third area calculated with pubosacral and widest transverse diameters as axes. Included among the 20 pelves there were 11 specimens with an outlet area below 88.8 ± 3.04 sq. cm., which was the mean outlet area by calculation found for a series of 65 Bantu pelves, and 9 specimens above this mean. In order to test Nicholson's formula to the full, some pronounced contractions of the outlet were selected for the experiment. The range of planimeter areas for the group of 20 specimens was 68.1 sq. cm. to 119.6 sq. cm.

Ten areas calculated by Nicholson's formula were less than the planimeter area, and 10 were greater. Twelve calculated areas showed an error of less than 4 per cent, 5 an error of less than 7 per cent, and 3 an error of more than 10 per cent. The error in the last 3 areas was -11.3, -11.4, and -19.4 per cent respectively. A discrepancy of this size is serious and calls for consideration. The planimeter areas for these 3 outlets were respectively 100.9, 72.0 and 68.1 sq. cm.; and the corresponding areas calculated from the pubosacral and widest transverse diameters were 103.9, 72.3, and 68.0 sq. cm., showing a very close correspondence.

In the majority of outlet tracings the interischial spine diameter was less than the maximal transverse diameter which lay anterior to the former. The reason for the near approach of the calculated to the true area is to be found in the fact that the anterior portion of the tracing tends to be angular, and not rounded as in an ellipse (see Fig. 2). Therefore, what is lost in the reduced length of the interspinous diameter is gained in the virtually increased length of the pubosacral diameter. If, then, inspection of the A.P. film shows large projecting ischial spines, it will suggest that the calculated area of the outlet may be smaller than the true area. But an impression of the forepelvis must be got from the film: if there is marked narrowing or angularity, this feature will counteract the effect of the unduly shortened transverse diameter in giving a negative error for the outlet area. There are very few exceptions to the general observation that the forepelvis has the same shape at the level of the outlet as at the brim. Another guide, though not so constant, is the association of a narrow pubic arch with a narrow forepelvis at the outlet.

To summarize, one cannot depend on an accuracy within the limit of a 10 per cent

error in calculating the area of the outlet. It is thought that greater errors can certainly be avoided by paying attention to the encroachment of the ischial spines on outlet space, and correlating this with the width of the forepelvis. It may be stated that several modifications were devised to overcome the possible error, but no satisfactory solution was found.

The diameters representing axes of the ellipse. Having shown that by calculation the error limit for the area of the inlet is well within 5 per cent, and for the area of the outlet within 10 per cent, the measurements to be derived from the X-ray film are four in number. The conjugate and transverse diameters at the brim are measured and corrected according to their known height above the film: from them both the area and the brim index are calculated. The derivation of the two outlet axes was more difficult, and they must be considered in some detail.

1. *The interischial spine distance.* The intention was to obtain this diameter from the A.P. film, thus avoiding a second exposure. The difficulty is to find the height of the ischial spines above the table or film.

Thoms⁶ method with a lateral view is favoured by many in the United States. The two spines appear on the lateral film at different levels and of different sizes because they are not equi-distant from the film. Thoms then gets the vertical height of the diameter by making it pass horizontally midway between the two spine levels, and measuring on a scale placed in the midline by the natal cleft. It can easily be shown that the point midway between the spines does not lie on the level of this interspinous diameter, and the method cannot be accepted because the error may sometimes be appreciable.

Paul Cave's⁷ and Nicholson's⁸ methods are mathematically sound, but require several exposures and more calculation

than in our method. In some cases Cave's vertical shift does not give accurate results, and the reason may be found in the fact that small differences of length resulting from the shift are particularly unreliable unless the shadows are not only very clear, but equally clear. In experimental work on Cave's method we have found that the ischial spine height is level with the table in cases in which it was known to be in the region of 3.0 cm. above this level. While it was thought that this vertical shift method would be very useful to have recourse to when great accuracy was desired, our observations have led to disappointment in the possibilities of this technique.

It occurred to us that the ischial spines might be at a fairly constant height above a table supporting the pelvis placed so that the brim is horizontal. Measurements were made on 60 dry pelves, and this ischial spine height when the inlet is horizontal was found to be remarkably constant. For the 60 observations the range was 1.7 cm. to 3.7 cm. (only 3 were under 2.0 cm.), with a mean of 2.71 ± 0.13 cm., and standard deviation 0.52 cm.

In the method of this paper the focus-film distance is 100 cm., and the film lies 7.0 cm. below the table surface. Thus the ischial spines would be 7.91 cm. above the film on the average. In our calculations this figure has been made 10.0 cm., which means that the film interspinous diameter must be multiplied by $(90 \div 100)$ for correction. If one errs by 1 centimetre in the height of the spines—and this is shown to be the maximal error possible—there will be a 1 per cent error in this diameter of which the length is of the order of 10.0 cm. Therefore, our theoretical error here is only of the order of 1.0 mm.

Finally, with a horizontal brim the ischial spines are invariably visible on a good film, not being overshadowed as in some positions.

2. *The pubosacral diameter.* Even though it was discovered that the interspinous distance could be measured on the A.P. film, it was at first thought that a lateral view would be required for the determination of the pubosacral diameter. It was found, however, that the anterior extremity of this line on the film was indefinite. Experiments were carried out by placing opaque markers on the under surface of the symphysis to serve as a guide in measuring the required diameter. While at best the anterior point selected without a guide was arbitrary, an error of 1 centimetre and more was found to be frequent. In fact, the situation of the true point was so unexpected that, unless observation is supported by practice with guiding markers, a mistake is probable in most cases. It was concluded, therefore, that X-ray measurement of the pubosacral diameter was of no value. Direct measurement with callipers seemed to offer greater accuracy, and would avoid the necessity of a lateral view film.

Clinical measurement is possible only from the posterior surface of the sacrum, though the under surface of the symphysis is easily palpated. It is usual to subtract 1 centimetre from the length obtained to get the true pubosacral diameter. This matter was investigated by measuring 60 dry female Bantu pelves, and the difference between these two diameters—one from the posterior surface of the last piece of the sacrum and the other from its anterior surface—was found to have a range of 0.5 to 1.5 cm. The mean figure for the 60 specimens was 0.92 ± 0.5 cm. with a standard deviation of 0.21 cm.

For practical purposes, then, 1 centimetre may be subtracted from the clinical measurement to give the true pubosacral diameter. The roof of the sacral canal is usually felt without difficulty, and the measurement is taken from the depression

below it to the posterior aspect of the under surface of the symphysis pubis.

It is unfortunate that this important diameter cannot be obtained with any precision radiographically. Nicholson's method is probably the only one which affords any approach to accuracy. While his technique for finding the length in question is theoretically superb, the capricious behaviour of X-ray shadows frequently defeats one here as in so many other instances. Experiments were performed to discover whether the anterior or posterior surface of S5 was seen on the film, when the patient sat forward as in the Chassard and Lapine pubic arch method.⁹ The findings became significant only when experiment was transferred to patients. The lower sacrum frequently curves inwards so sharply that some part of it above its tip throws the outermost shadow. In effect the tip of the sacrum is overshadowed by some part of it higher up; and unless the film is of unusual quality, identification of the requisite shadow will be impossible. It is impossible to state precisely what error occurs here, as the curvature of the sacrum is variable; but it is unlikely that radiological measurement is superior to direct clinical determination of this diameter.

PART II.

Before describing the radiological method of pelvimetry recommended, certain fundamentals must be established. Experiments were performed to determine the surface markings of value, and the position of the patient when the brim plane is horizontal. These observations are described in the following section.

OBSERVATIONS.

Spine of L5. Our radiological experiments have shown that when the superior

strait is horizontal a prolongation of the conjugata vera runs through the spine of the last lumbar vertebra. This means that the inclination of the pelvis which now is zero can be measured from the 5th lumbar spine, or that the promontory is at the same level as the 5th spine. In the erect posture, however, the conjugata vera produced passes between the spines of L2 and L3, though this will vary according to the pelvic inclination in the subject concerned.

The tip of the 5th lumbar spine, therefore, is at the same level as, or slightly below, the sacral promontory. It is widely recognized that in the majority of cases the promontory lies above the level of the brim as determined by the iliopectineal lines. It is, therefore, more correct to use the 5th lumbar spine than, as frequently suggested, the 4th for the posterior point. According to the method here suggested, the encroachment of the promontory on to the plane of the brim is disregarded in finding the area and brim index. Hence the actual level of the promontory is a matter of indifference. But it is submitted that the 5th lumbar spine is as near to the level of the brim as any vertebral point that can be found; and where there is a slight difference, the error will be so small as to be negligible for practical purposes.

There is some danger of error in finding the surface marking for the 5th lumbar vertebra. This error is unlikely to be more than 2.0 cm. The probability is that a spine higher than the 5th, rather than a point lower, may be chosen. In the first place bony projections on the posterior aspect of the sacrum are not so prominent as the lumbar spines; and in the second, difficulty will be found with a satisfactory semi-recumbent position in getting points well below the 5th spine to the same horizontal level as the symphysis. Our experiments have shown that in the few cases in which

inaccuracy occurs the result for the length of the conjugata vera is only a few millimetres. Some experimental results will now be given because there is confusion on this problem, as in the statement quoted from Jacobs.¹⁰ Even Thoms¹¹ in "The Obstetric Pelvis" fails to state the position correctly: if the point used for the last spine is 2 cm. higher than the spine itself, the brim plane cannot be said to be 2 cm. lower than it is thought to be. The conjugate in this case is oblique to the horizontal, with the last lumbar spine situated 2 cm. lower than the symphysis.

Geometrical drawings show that with a film-focus distance of 100 cm., if the marker on the patient's back were to be placed 2 cm. above the correct point (last lumbar spine), the error in the final result for the conjugate is on the average almost exactly -2 mm. But if the marker were placed 2 cm. lower than the correct point, there would be no error in the final result. (In the second case the shadow is distorted with loss of length due to obliquity of the conjugate, but the distance between object and target is less than before. This compensates for the loss in length due to obliquity.)

To apply these principles in practice a dry pelvis was taken and a wire fixed in the position of the true conjugate. This wire was measured because the conjugate itself is unreliable for the purpose. It will be obvious that we bring our supposed lumbar 5 point to the same level as the symphysis in practice. Therefore the height of the symphysis gives the object-film height.

Testing of Surface Anatomy Errors in X-ray Views of a Parallel Brim.

- (I) Brim horizontal: height above film 18.5 cm.
 Length of wire on film = 14.5 cm.
 \therefore Length of wire = 11.82 cm.
- (II) Brim oblique, with symphysis higher. Symphysis height above film 21.8 cm.

Height difference between symphysis and L5 spine: more than 4.0 cm.

Length of wire on film = 14.0 cm.

\therefore Length of wire = 10.95 cm.

Error - 0.87 cm.

- (III) Brim oblique with symphysis lower. Symphysis height above film 15.0 cm.

Height difference between symphysis and L5 spine: more than 6.0 cm.

Length of wire on film = 13.2 cm.

\therefore Length of wire = 11.22 cm.

Error - 0.60 cm.

Length of wire = 11.9 cm.

One may accordingly conclude as follows:

With posterior point 2 cm. too high,
 error = - 2.0 mm.

With posterior point 4 to 5 cm. too high,
 error = - 8.7 mm.

With posterior point 2 cm. too low,
 error = 0

With posterior point 6 to 7 cm. too low,
 error = - 6.0 mm.

Semi-recumbent position. Great difficulty was encountered in placing the patient in such a position as to obtain a horizontal brim. Experiments were conducted on students and patients to solve the difficulty. As pointed out above, the posterior point is frequently lower than the anterior when the semi-recumbent position is such that the normal ray strikes the brim without passing through the upper abdomen or thorax. If one arranges an effective Walcher position with the subject's lower extremities hanging well over the edge of the table, the pelvis is tilted forward so as to bring the brim horizontal with the woman lying well back. But the Walcher position cannot be used on a standard table. It was found that, if the subject arched her back so as to give a moderate lumbar lordosis, our point was gained: the symphysis was depressed, the 5th lumbar spine raised, and when these two were in the same horizontal plane the patient was still lying sufficiently far back to allow the incident ray to miss the upper

abdomen in women during the first half of pregnancy. It is important to realize that in whatever position the patient is placed, an incident ray at right angles to the brim has to traverse the same amount of tissue. Nothing is to be gained by having the brim in a plane inclined to the horizontal and arranging the tube at a right angle to this plane.

Radiographic Technique.

Equipment: Standard table. Adjustable back-rest that can be bolted to table. Foot-support that can be bolted to table. Centimetre rule and callipers. Dividers or sliding compass for measuring on films. Standard equipment for exposing and developing films.

Exposure: An exposure of $3\frac{1}{2}$ to 4 seconds during the first half of pregnancy, and 4 to 6 seconds for cases in the last 2 months of pregnancy.

Setting: During early pregnancy we have used a kilovoltage of 75 K.V.P. and a current of 80 M.A., and as gestation advances this is raised to 80 or 84 K.V.P. with current 80 M.A.

METHOD.

The A.P. view is the one on which we rely for all our information; but, if the sub-pubic angle is considered narrow, a second film is exposed as in the Chassard and Lapine⁹ method.

(a) The brim must be brought into a horizontal plane. A small strip of adhesive tape is placed over the spine of the last lumbar vertebra, and the patient made to sit back against the back-rest at an angle of over 45 degrees. In order to get the posterior point and the upper edge of the symphysis pubis in the same horizontal plane, the patient has usually to arch her back considerably, only head and shoulders being in contact with the rest. The knees are extended, and the feet pushed against the foot-support. The height of the adhesive strip from the table is measured with the limbs of the callipers

crossed, and checked against the height of the symphysis. The lordosis is then regulated until the two heights are equal, the patient instructed to keep still, and the film exposed. A Potter-Bucky diaphragm is used. The height obtained is read against the centimetre rule. To this is added the height of the table surface above the film and thus we have the object-film distance.

The focus-film distance used is 100 cm., but if the apparatus used does not give clear films in late pregnancy, a distance of 75 cm. will give better results. The 100 cm. distance affords simplicity in calculation. The target is centred over what is estimated to be the mid-point of the brim plane (about 6 cm. posterior to the symphysis), a plumb-bob being useful for the purpose.

From this film the interspinous and brim diameters are derived, and the shape of the brim studied.

(b) Excellent radiographs of the pubic arch are obtained by sitting the patient at one end of the table directly on a cassette covered by a Lysholm grid. The legs, well separated, come over the table edge with the feet supported on a stool, and the trunk is bent forward as low as possible. Personal trial of this position will show that the pubic arch lies against and parallel to the grid. Any target height may be used. We use 100 cm. because we know the approximate error, which in practice is negligible. If it is wished to reduce the relative over-exposure of the lower portion of the sacrum, shading may be done with an opaque mask.

From this film are obtained the height of the symphysis, the depth of the pelvic basin, the intertuberos diameter, and the subpubic angle.

Correction of film measurements. The principle involved is geometrical, similar triangles having certain sides and bases proportional. If the object-film distance is 18 cm. the distance from target to object

is (100-18) or 82 cm. The quotient of the sides of the triangle is, therefore, $82/100$ or 0.82, which is the factor by which the film diameter has to be multiplied to find the true diameter.

It has been shown that ischial spine apices are always 3 cm. from the table. We use a table of which the surface is 7 cm. above the film. Thus the spines are 10 cm. from the film, or 90 cm. from the target. In this way the interspinous distance of the film is always multiplied by 0.90. If the table-film distance happens to be 6 cm., the spine-film distance would be 9 cm., and the factor necessary for correction would always be 0.91.

This correction of film measurements is unavoidable. However, with a target-film distance of 100 cm. the calculation has been reduced to its simplest possible form. No correction is required for the pubic arch measurements suggested. The arch is virtually in contact with the film, and for this reason both film and true proportions are very nearly equal.

As it is parallel to the film, the subpubic angle will be unchanged. The symphysis error is about 1 mm. and so is the depth of the pelvic basin if measured in the anterior midline to the top of the symphysis. The anatomical depth is measured from the lowest part of the ischial tuberosity to the brim as a tangent to the anterior curve of the acetabulum, and the error may be up to 3 mm. increase in length. The intertuberous diameter is somewhat arbitrary even on skeletal material, and on the film must be measured a few millimetres above the lowest points of the tuberosities. The technical error will make the film measurement too long by not more than 5 millimetres.

In calculating the area of the planes of brim and outlet, the formula for an ellipse is used, i.e. $\text{area} = \pi a b$ (where the axes measure $2a$ and $2b$). In practice one would

multiply the product of the two diameters by $11/14$.

The brim index is given as a percentage of the antero-posterior diameter divided by the transverse, but this will be discussed later.

DISCUSSION OF RESULTS.

1. Experiment with dry pelves has shown that the interspinous distance obtained by this method is extremely accurate. The pubic arch measurements have an accuracy which is adequate for practical purposes, and there is no likelihood of significant errors, nor have we used any clinical method which gives comparable results. As stated above, the pubo-sacral diameter can be measured clinically with the same accuracy as on a radiograph. Pelvimeters do not usually measure in millimetres, and it is best to measure with a pair of callipers and get the distance on a centimetre rule. It has been found convenient to reduce the curve of the limb of the callipers that makes contact with the symphysis. The patient lies in the left lateral position with the right thigh abducted. The roof of the sacral canal is palpated and the measurement is made from the depression below it to the posterior aspect of the under-surface of the symphysis pubis.

Working in conjunction with a colleague, it was found that we varied by a few millimetres in measuring the pubo-sacral diameter. Without due care, an error of a centimetre may occur in some cases. The important features are finding the hiatus sacralis, and the co-operation of the patient.

2. The brim measurements of patients were tested by using Cave's method⁷ with a vertical tube shift, and exposing two films. The results obtained showed a close correspondence for the two methods, but the object film (OF) distances did not correspond. The transverse of the brim was

the diameter chosen for comparison, because its extremities on the film are constant. The OF distance in the case of pregnant women disagreed with the measured height of the superior strait by over 4 cm. in a few cases, but always by about 2 cm. This led to keen disappointment, until attention was directed to the ischial spine level and we found that by Cave's formula the ischial spines must frequently be at table level. Experiments were then performed on dry pelvises where the measurements are accurately known. Tube-film distances of 65, 100, and 150 cm. were used, and the three possible combinations were worked out. The OF distances varied in the three calculations based on the interspinous distance, one result for the spine-table distance being 1.13 cm. when, in fact, it was 2.5 cm. This finding demonstrates the weakness of Cave's method, for whatever purpose it may be used: the differences in object length (diameter) are very small; and apart even from errors in measuring, the definition of shadows on different films may vary sufficiently to give false differences.

The transverse diameter of the brim proved a much better standard for experiment, for in all three calculations both its length and its OF distance showed differences of not more than a small fraction of a millimetre. Both in the case of skeletal material and patients there were two discrepancies which were constant: the OF distance was always less on calculation (Cave) than on direct measurement, and my corrected figure for the diameter was always less than the one obtained from the Cave formula. The following extract from my notes explains the situation. "Pelvis A.445.519; transverse 10.76 cm. (Cave); and 10.54 cm. (Heyns). When measured on the pelvis the transverse of the brim is well over 11.0 cm., however small the diameter is made. The discrepancy in the OF value

must be due to the showing on the film of a circumference which lies deeper than the brim, i.e. somewhere about the level of the plane of the cavity. This would explain (1) why OF is nearly 2 cm. shorter than the true value, and (2) why the transverse is shorter than it should be."

On the clear, perfectly exposed films of skeletal material one can see, at the widest part of the ilium in superior relation to the ischial spines, a narrow white strip of compact bone separating the brim outline from the cancellous bone detail of the iliac fossa. In superior films the lateral border of this strip, which is only a few millimetres wide, can sometimes be traced as the continuation backwards of the ilio-pectineal line. The truth of this was confirmed by finding that the correct X-ray measurement as well as the OF value corresponded very closely with these distances on the dry pelvis.

Examination of the iliac portion of the brim in a funnel pelvis will show that a projection of the brim is likely to be overshadowed by the massive bone lying around it, particularly the great depth of bone lying on its medial side. This medial bony incline is, in fact, represented on the film by the dense white line. In effect, therefore, the bone representing the brim—whether this be the iliopectineal line or a line medial to it on or about the brim level—lies in the substance or shadow of a wide shelf of bone; and, as there is no particular density or prominence about this line, it would be unreasonable to expect it to show up on the X-ray film. In the majority of pelvises there is an inward slope of this portion of the ilium towards the ischial spine tips, and an inspection would make it clear why the curve on the film represents the shadow of a pelvic level much deeper than that of the superior strait. Two points must be noted: firstly, the above observations apply to the majority of pelvises because there is in them a convergence of the lateral

walls in descending from the superior strait plane; and secondly even perfect exposures do not from necessity show the iliopectineal line in the form of the lateral margin of the dense white strip mentioned above, because this margin is variable. We discovered early that the Roentgenogram never gave the anatomical iliopectineal line as a marking, and that what the film showed as the innermost margin of the iliac portion of the true pelvis was in fact medial to a wire running along the iliopectineal line itself. But we never suspected that this innermost margin of the film represented bone lying near the plane of the cavity of the pelvis.

3. In view of the above observations, it became necessary to investigate the effect on measurements of under-exposure of films and possible distortion from scattering of rays. The changes found were of the order of a fraction of a millimetre and are, therefore, of no practical significance. Even though the experiments could not be performed with mathematical precision, and measurement on films in fractions of millimetres is unreliable, a few experimental results will, nevertheless, be tabulated here, because they are believed to be relevant to the problem.

In the poorly exposed films it was quite

EXPERIMENT I.

Under Exposure of Films in Case of Bony Pelvis (A.445.519).

| Focus-film distance (cm.) | Transverse of brim (cm.) | | Inter-ischial spine distance (cm.) | |
|---------------------------|--------------------------|---------------|------------------------------------|---------------|
| | Under-exposed | Fully exposed | Under-exposed | Fully exposed |
| 150 | 11.74 | 11.80 | 10.60 | 10.60 |
| 100 | 12.33 | 12.40 | 10.93 | 11.00 |
| 65 | 13.40 | 13.50 | 11.53 ± | 11.55 |
| 65 (minimum exposure) | 13.38 | | 11.53 | |

We submit, therefore, that the iliopectineal line or brim of the true pelvis cannot be shown on a Roentgenogram. When radiographing skeletal material good definition is obtained, and the lateral margin of the well-defined white strip on the body of the ilium is a near approach to the anatomical brim of the lesser pelvis. This white strip does not show up in the films obtained from patients, and it will be shown how a superimposed foetus obliterates this shadow. It is submitted, further, that the iliac portion of the radiographic brim is on the average a shadow of the bone approximately at the level of the lower margin of the obturator internus muscle arising from the body of the ischium. These findings were unchanged when stereoscopic examination was done.

impossible to see the white strip, and the longest diameters obtainable were those shown in the first column of Experiment I table.

A foetus was superimposed on a dry pelvis to test the effect of distortion on measurements. A difference could not be detected. If, however, we take the transverse of the greater curve encompassing the white strip, there is a marked difference due to the fact that the foetal head overshadows one side of the curve (Experiment II). On this side the white strip disappears as entirely as in the under-exposures.

A block of paraffin wax was superimposed on the same pelvis for scattering effects and exposures made at 100 cm. With a full exposure the transverse was 12.35 cm., and with an under-exposure 12.30 cm.

EXPERIMENT II.

Greater Circumference of Inlet on Films (A.445,519).

| Focus-film distance (cm.) | Transverse of brim (cm.) | |
|---------------------------|--------------------------|-------------------------------|
| | Plain pelvis | Foetus superimposed on pelvis |
| 150 | 12.40 | 12.10 |
| 100 | 13.10 | 12.63 |
| 65 | 14.10 | 13.70 |

For the above experiments the object photographed and measured is indefinite as follows (Experiment III).

EXPERIMENT III.

| Tube shift (cm.) | Diameter (cm.) | OF value (cm.) |
|------------------|--------------------|--------------------|
| 100 and 150 | 14.95 (error 0.05) | 17.40 (error 0.40) |
| 65 and 100 | 15.18 (error 0.18) | 16.15 (error 0.85) |
| 65 and 150 | 15.03 (error 0.03) | 16.63 (error 0.37) |

in the sense that it has variable extremities which cannot be recognized. The tests were accordingly repeated with a metal ring as object. Difference was not detectable between the measurements of the plain ring and those with a foetus superimposed. The result of correction by our own method and that of Cave will be given to show how the accuracy of the latter method is impaired, because the act of measuring has to be more precise in Cave's method than in our own.

The internal diameter of the metal ring was 15.0 cm., and the measured OF distance was 17.0 cm. Exposures were made at 150, 100, and 65 cm.

At 150 cm. the ring diameter on film was 16.91 cm.

At 100 cm. the ring diameter on film was 18.10 cm.

At 65 cm. the ring diameter on film was 20.20 cm.

Correction for the diameter is as follows:

At 100 cm. — $18.10 \times 83/100 = 15.023$.
(0.02 cm. error)

At 150 cm. — $16.91 \times 133/150 = 15.00$ (0 error).

At 65 cm. — $20.20 \times 48/65 = 14.91$
(0.09 cm. error).

With the three vertical shift combina-

It can be seen from these figures that the Cave calculation gives an error which is considerably greater than that of the simple method.

CONCLUSIONS.

After an exhaustive consideration of details of current radiological technique in assessing the capacity of the female pelvis, it is necessary to state what in the present state of our knowledge can be demanded of X-ray pelvimetry.

First the area of the outlet (plane of least pelvic diameter) can be found. The error may be as high as 10 per cent, but it has been shown when such a high error may be expected and how to aid correction. While it is unfortunate that the antero-posterior diameter cannot be precisely estimated by any radiographic technique, the measurement can be made directly with callipers with an accuracy to the nearest 2 to 5 mm.

Second, if it is considered necessary or desirable to have a picture of the pubic arch, the technique is particularly simple, and the results indeed the most reliable

that Roentgenography can provide. The measurements of symphysis, intertuberos diameter, and depth of the pelvic basin vary by about 1 mm. from the true ones, and the subpubic angle is unchanged.

Third, the calculation of the area of the pelvic brim plane was an important objective of the investigations reported here. The results of such a study on a collection of skeletal material are given in Part I. Roentgen studies have, however, shown that by our method the greatest transverse diameter of the brim cannot be found, and we submit that this is not possible by any method, stereoscopic or otherwise. Experiment has shown that intra-pelvic space as seen in the A.P. view is encircled by a shadow of bone which is not, as has heretofore been imagined, the iliopectineal line. The lateral portions of the girdle seen on the film represent the bony wall at or about the depth of the plane of the cavity of the pelvis. Anteriorly the iliopectineal line is clearly demarcated for varying distances. Its continuation even as far as the iliopectineal eminence is frequently stimulated by the anterior and posterior margin of the obturator foramen, the outer or inner edge of the superior aspect of the superior pubic ramus, and osseous ridges near the ischial tuberosities. But it is not the purpose of the present communication to enlarge on this question of anatomical details which complicate the interpretation of films.

It has frequently been stated that the true conjugate lies at a higher level than the transverse of the brim,^{12, 7} and this is universally recognized to be true for pelves excluding those with four-piece sacra and a small percentage of specimens with five-piece sacra. In X-ray pelvimetry this observation must now be recognized to have lost its importance, in spite of the fact that an accurate estimation of the conjugate length can be gained from a lateral view film on which the anterior part of the

sacral promontory is invariably visible. The anteroposterior diameter of the A.P. view excludes the greater part of the promontory, all of which cannot be shown on any film, whatever its quality. What is seen posteriorly of the termination of this diameter is at the level of the 2nd sacral vertebra in a high preponderance of pelves.

For these reasons we may estimate the area of a plane narrower than that of the superior strait by taking into consideration only the intra-osseous space of the film seen as an interrupted curve. If previously we considered the major portion of this curve to be a shadow of the brim, we may have the consolation now that it is a narrower part of the girdle, and is at least of more significance in obstetrics than a wider plane above. The anatomist has directed his attention to the brim, to the neglect of the plane of the cavity. For academic reasons it would have been gratifying to collaborate with the anatomist in the radiological field, but even if the Roentgen ray has failed us here it has given its virtue to the obstetrician. The pelvic brim index of Turner cannot be used in radiographic work, but a similar index may be used for the cavity plane we have been discussing. This cavity index is likely to give a slightly higher figure than Turner's, and for 50 Bantu antenatal and postnatal women it gave a mean of 91.28 against a female Bantu mean for skeletal material of 90.4 (65 pelves). One is diffident about making new recommendations, but it may be of value to follow the argument a little further for the brim index and area. Certain possibilities for these values immediately present themselves once there is recognition of the fact that the skiagram will give an index and area for the cavity plane only.

It appears, from the observations at our disposal, that the greatest transverse of the brim obtained from A.P. films is in the region of 7.5 mm. shorter than on the pel-

vis, the range being from 5.0 mm. to 10.0 mm. The conjugate diameter of the film, in which we disregard the promontory, shows a gain posteriorly. In the 60 pelvises studied in Part I dioptrigraphic tracings were made (see Fig. 1), and the antero-posterior length from the anterior surface of the promontory to the modified curve posteriorly was measured. The mean for this distance in 60 pelvises was 14.7 ± 1.13 mm., with a range of 5.0 mm. to 25.0 mm., and standard deviation 4.36 mm. The gain in the conjugate is thus 14.7 mm. The distance from the iliopectineal line on the symphysis was measured to the most posterior portion of the symphysis shown on the skiagram. In 50 antenatal and postnatal Bantu women the mean for this distance was 13.1 ± 0.52 mm., with a range of 9.7 mm. to 19.1 mm., and a standard deviation of 1.83 mm. Considering the innermost girdle of bone which is shown by the X-ray to enclose space, we have an antero-posterior diameter which on the average, compared with the conjugata vera, suffers a loss of 13.1 mm. anteriorly and a gain of 14.7 posteriorly. This mean would apply with accuracy to a series of measurements, but may err considerably in a specific case. For a series, therefore, this X-ray conjugate can be said to be almost equal to the anatomical true conjugate. As, however, the X-ray transverse diameter is about 7.5 mm. shorter than the brim transverse, the index derived from (film conjugate \div film transverse \times 100) should be a little higher than the Turner brim index. It would be valid to state that this index is of value, because the bulk of the figures in future will be derived from radiological observations. Whereas the few have studied skeletal material, increasing numbers of observers will be reporting X-ray findings. Moreover, the index here analysed bears comparison with the Turner index itself, in spite of the fact that the two

values are for slightly different levels of the lesser pelvis. In our observations, the mean Turner index for 65 female Bantu dry pelvises was 90.4 ± 2.0 , S.D. 8.2, and range 69.6 to 104.4. In the suggested X-ray index the figures for 50 Bantu antenatal and postnatal women were: mean 91.28 ± 1.7 , S.D. 6.0, range 79.1 to 110.8.

If it is desired to calculate the area of the brim plane in a particular pelvis, but with greater precision for a series of pelvises, the modification necessary is based on the following observations: the transverse axis of the ellipse is approximately 7.5 mm. too short, and the anteroposterior axis is of the correct length. If the latter axis is measured anteriorly on the film to about the middle of the posterior surface of the symphysis pubis—rather as in measuring the "obstetric" conjugate on skeletal material—we gain half the width of this pectineal shadow which on the average is 13.1 mm. Thus, in this modification a figure for the anatomical brim area is very closely approached.

Apart from studies during labour, it is difficult to see that a lateral view film can contribute much to our knowledge of any pelvis concerned in an obstetric prognosis. The true conjugate can be found, but is of negligible value taken by itself; and much is made of the greater sciatic notch by some obstetricians. Academically this notch is of unbounded interest and importance, but in practice it is only of indirect value in showing how long the iliac portion of the inlet is. This can be seen directly in the A.P. view with greater certainty and here too the distance of the ischial spines from the sacrum will give all the information of practical value. The early workers made curious statements about X-ray plates showing the thickness of the sacrum, "the presence or absence of atrophy of the sacrum or of sacro-iliac ankylosis" (Pinard and Varnier¹³), and so on. These men

were pioneers and deserve only our admiration, but one feels that we have not advanced since their time, when we insist on the necessity of seeing the sacro-sciatic notch radiographically. One submits that the clinician can derive from the A.P. view with horizontal brim all that the Roentgen ray can teach about the average pelvis, that a photo of the pubic arch will be required in some cases, and that a lateral view will be taken to complete the information required only in special cases.

PART III.

THE PRESENT-DAY STATUS OF X-RAY PELVIMETRY.

When Varnier and Chappuis¹⁴ in 1896, first radiographed the pelvis, an era of great promise for obstetrics was opened. The half-century which has followed, though a period of intensive research in many branches of knowledge, has failed to bring the conviction that every primigravida should have the pelvic girdle radiographed. For this diffidence on the part of the accoucheur there are several reasons which in no way reflect on the inconvenience, danger, or cost to the patient. Whereas the pioneers mentioned required exposures of 3 hours to gain pelvigraphs from the cadavera experimented upon, and the first pelvic skiagram of the living subject was obtained with an exposure of 45 minutes, the patient of to-day is detained by the radiologist for a total period of about 10 minutes. The danger to the mother and foetus is negligible, and the cost for obtaining two views is less than that of a blood count. The obstetrician recognizes his conspicuous limitations concerning the prognosis in a case of disproportion, but he would gain small comfort from the possession of an indifferent X-ray picture of the pelvis in question. He is unable to

use this shadow and, even if it were accompanied by some measurements, he is distrustful of such phantasies. It is, however, dawning on him that he must be considerate of this handmaiden who has taught him much that he can learn in no other way; and as his understanding increases he will return with a fuller knowledge of what he should seek to discover from this source. The momentum which radiology can give to advancement in the study of parturition is reciprocal to what obstetrics may demand of radiology. Until there is a universal employment of X-rays in this sphere, we shall progress but slowly; for it is submitted that we do not yet know the pelvic factors that are essential to eutocia, and that the skiagram is the only means to bridge this gap.

Much is written about X-ray pelvimetry, and many methods are advocated. The obstetrician is dazzled by performance and complexities which are hurled at him rather than given to him. He is not an investigator, but has a sincere desire to enlist such aids as he understands. It is necessary, therefore, to avoid complexity and, if possible, to provide methods which he can personally carry out.

Now there are two shades of opinion born of the mysticism of pelvic radiography. Whereas it has always been possible to measure the intact pelvis approximately, it was impossible to gain an impression of its architecture until X-ray photography came into being. It was novel, but incidentally easier, to assess a pelvis on morphological grounds—and thus we have a vogue. The older approach to pelvic capacity was based on mensuration, and X-ray pelvimetry was a natural gradation. But this new pelvimetry was ill at ease, and some of its adherents resorted to the study of shape and form instead. It seems desirable to have a full knowledge of our subject and not to abandon the more precise moiety,

even if at the moment we are unable to equate the values of mensuration.

Albert¹⁵ seems to have been the first to suggest that the pelvic brim should be parallel to the film lest diameters in this plane be distorted. This obvious basic principle was neglected for a generation for reasons that can only be surmised. In the early days there was no Potter-Bucky diaphragm, and good pictures were only rarely obtained. For many years measurements were obtained by comparison with a standard dry pelvis X-rayed in the same position as that of the subject. Varnier¹⁶ used a focus-film distance of 5 metres in order to enable him to take measurements not requiring any correction. Orley¹² states that Varnier succeeded in obtaining an outline of a dry pelvis at 25 metres distance with an exposure of only 10 minutes. But technical difficulties must have been so formidable that it is not surprising that Varnier's teleroentgenographic method never found favour. It is necessary to point out that as early as 1897 Levy and Thumin¹⁷ used the so-called mathematical method: their simple equation contained as one factor the cosine of the angle of pelvic inclination!

In the simpler mathematical methods, because certain measurements such as the height of the brim above the film had first to be made, there was a lack of precision. Precise methods were, however, evolved, and in 1924 Blanche and Portes¹⁸ devised a simplified technique which was mathematically accurate. It is shown elsewhere in this paper that, nevertheless, there is a liability to error in practice, while for the clinician too many exposures of film may be required. Paul Cave⁷ modified the method of Blanche and Portes, and shows how the object-film distance may be calculated with precision if two films are obtained, after making a vertical shift of the tube for the given object. Hastings¹⁹

described a similar method, using a horizontal side-to-side shift. For certain practical purposes it is reassuring to be able to fall back on accurate methods such as these, but for general use workers will begrudge the expense and trouble involved.

Stereoscopic methods had been favoured by some investigators, but only when Moloy²⁰ described his precision stereoscope did it become generally known that the stereoscopic image could be measured. While the principles underlying Moloy's technique had been in use for many years, the difficulty lay in imitating in the stereoscope the set of circumstances that prevailed during exposure of the films. By Moloy's ingenuity the technique was standardized in the design of his instrument. Caldwell, Moloy and their co-workers^{21, 22, 23, 24} have concentrated their attention on foetal pelvic relations during labour: their studies are predominantly concerned with pelvic architecture, and where they anticipate disproportion the image of the pelvis is measured in space. The radiography during labour is unquestionably of great value, but the expense and labour involved put their methods out of reach of the average clinician. It may also be doubted whether stereoroentgenography of this kind will be the method of the future, although to the investigator it will always be of advantage, an assumption borne out by the importance of the discoveries made by these workers.

Measurements obtained from the precision stereoscope in which an antero-posterior tube shift is employed are not universally accurate. The "phantom ruler" must be held exactly in the plane to be measured, and when the diameter concerned is the conjugata vera one has even to know the slope of the plane, it being impossible to be precise about this. By this method there is the same difficulty about seeing the promontory shadow as

exists in other anteroposterior views, and the impossibility of seeing the true transverse diameter of the brim is the same as described elsewhere in this paper. So much practice is required with this stereoscope that there must be a tendency to accept with reserve some of the measurements obtained.

With reference to the coronal plane used by Caldwell *et al.*^{21, 24} one cannot accept that if the ischial spines lie in this plane the greatest transverse diameter of the superior strait will always lie in this coronal plane. A study of skeletal material will show that this assumption is by no means always correct.

Nicholson's⁸ method is a stereometric one which is ingenious and theoretically accurate to the nearest millimetre, or as precise as the X-ray shadow enables one to be. He uses a stereometric shift of 10 cm. and obtains the true diameters not by viewing in a stereoscope, but by marking on tracing paper the stereometric shift of the terminal points of diameters required, and joining these points to the corresponding points at which the projection of the focus of the tube is shown. If a diameter lies in a plane oblique to that of the film this is detected by the shift of its termini being unequal. For the purpose of correction in this case, tables are presented. These films can further be used to give a stereoscopic view as relied upon by Caldwell *et al.* Nicholson's method of measurement requires more time for each case than does the precision stereoscope; but it can be used by anyone not possessing this instrument, and is certainly more precise and scientific.

Nicholson's technique demands two films for the inlet view, and two for the pubic arch. In the method suggested in this paper, one film only is required, and a second where the pubic arch is suspect. In the latter method there is greater simplicity

for the clinician, and his purpose is served equally. But the stereometric method is extremely valuable to have at our disposal, and there is much to be said in favour of its adoption by anyone but the occasional worker, i.e., by the investigator and workers in large obstetric hospitals. If Nicholson's paper has not met with the acceptance it deserves, it is because he has assumed too much in explaining the principles involved, both mathematical and technical. In studying the paper even a trained mathematician would have to spend an unjustifiable amount of time and thought on this method—and it has been published in a medical journal! It is, however, a method which has our full support. It was observed that this author published a paper in February 1943 on the same subject. Owing to war conditions that particular number of the journal failed to reach this country, and it has been impossible to follow any new ideas that may have been expressed by him.

Apart from stereoscopic methods there are the position methods, and here it is necessary to refer to some basic principles involved rather than to deal in detail with the technique employed.

In Thoms'¹¹ grid method we have sufficient accuracy for inlet measurements, provided we bear in mind the fact shown in this paper that the plane of the brim cannot be seen on an A.P. film. The technique has been found to be more cumbersome and to give results inferior to those obtained in the suggested method. Thoms'¹⁶ modification, in which he uses Rowden "pubic scales" and calculates the height of certain planes on a lateral skiagram, is mathematically unsound when applied to the ischial spines and comparable landmarks. While the latter error may not be great, he does not mention its range. The method of choice should be simple, with a clear statement of the limits of the possible

error, for it is imperative that too great an error be avoided even if occurring only in the exceptional case. Roberts²⁵ places the patient so that the brim is parallel to the film, and does not require a centimetre grid: the correction is made by the simple calculation used in the method of the present paper. Rowden²⁶ varies his technique from Roberts' in two respects: "pubic scales" are prepared for correction at varying distances of the inlet plane above the film, and the focus-film distance used is 4 feet 6 inches (preferably 6 feet). His exposure is for 25 seconds, the symphysis being shaded with a hatchet for half the time. The further the target is from the film the better, but an exposure of 25 seconds must result in too great movement on the part of mother or foetus.

Because our own method relies on a horizontal inlet, it is necessary to refer to some points made by Roberts and Rowden. Rowden²⁷ is in error when he states that a semi-recumbent position at an angle of 55 degrees ('it really ought to be $57\frac{1}{2}$ degrees') will make the brim horizontal. Even if the pelvic inclination in the erect posture be known in a given case, it is incorrect to think that the plane of the brim moves rigidly with the trunk. In passing from the erect to the recumbent position the individual describes a right angle, but the brim does not rotate through 90 degrees, because the recumbent position is usually associated with more lordosis than the erect. Similarly, when the patient leans against Roberts' back-rest there is a tendency to lordosis which would interfere with Rowden's mechanism for securing a horizontal brim at a 55 degree semi-recumbency. Rather than accept assumptions of this nature, the height of the pubic symphysis above the table and the height of the sacral promontory (spine of last lumbar vertebra) must in every case be measured and made equal, in order to be

sure that the inlet is horizontal. Unless the effect of lordosis is appreciated it will often be found that the patient is sitting straight up before the inlet becomes horizontal.

Rowden^{26, 27} assumes that the inlet is horizontal, and accordingly measures only the height of the symphysis above the table. Roberts²⁸ measures the distance from symphysis to X-ray tube. There is, then, a possibility that their inlets in some cases may be oblique and become appreciably distorted, and this is avoidable. Rowden²⁷ states categorically that, if a projection of the obturator foramina is not seen in this view, the position is correct. This is only approximately true. The brim can lie at a small angle to the horizontal without the obturator foramina appearing in this A.P. view; and conversely, in the exaggerated convergent android pelvis a part of the foramina may be seen posterior to the symphysis. The writer has observed this in skeletal and living material when there was no question of the brim being parallel. Rowden²⁷ gives his height of symphysis above table as 12.0 to 14.5 cm. ($4\frac{3}{4}$ to $5\frac{3}{4}$ inches). In our experience the range is from 10 cm. to about 13.5 cm., though the latter figure may later increase.

From Orley's¹² paper, and the discussion that followed, one gathers that he, and Martius, and Rowden are unaware of the impossibility of showing a radiographic shadow of the lateral portions of the iliopectineal lines. Martius is said to have evolved a method of calculating the surface of this plane. To this Orley objects and points out that on the average the transverse of the brim lies on a level lower than that of the conjugata vera. Rowden criticizes Orley's statement, and suggests that a 6-foot focus-film distance will nullify the effect of the error of the two planes. Whatever variation is adopted to correct the figures, it is of some importance to realize that one does not see the anatomical inlet

on the film, but a level which lies close to the plane of the cavity.

Roberts²⁸ refers to the importance of measuring the oblique diameters of the brim accurately. To ascertain the presence of asymmetry of the brim one would inspect it and, when necessary, measure the two oblique diameters. The iliopectineal eminence is so large a mass of bone that even on the dry pelvis the oblique diameter is difficult to standardize. One recommends, therefore, that for comparative purposes the diameter be measured from the sacroiliac joint to a line drawn parallel to the line joining the tips of the ischial spines—preferably a line in the region of the iliopectineal eminences. He also demands an accurate measurement of the pubosacral diameter in some cases, suggesting the Chassard and Lapine⁹ technique. It is shown in this paper that the antero-posterior diameter of the outlet cannot be measured radiologically, not even on the lateral skiagram, although theoretically Nicholson's stereometric method approaches accuracy very closely even in this instance.

Jacobs¹⁰ brings the film parallel to the superior strait after measuring the pelvic inclination with his inclinometer. The principle underlying his method is good, but one is doubtful of the accuracy of his inclinometer. In the first place he has to measure the width of the symphysis pubis directly, an error of $\frac{1}{2}$ to 1 cm. being readily made. Secondly, he cannot often feel the sacral promontory in the supine position with thighs unflexed, and must rely on his judgment for the direction in which the inclinometer rod is passed through the vagina. Thirdly, the inclination of the superior strait does not necessarily rotate through the same angle as does the body to reach the supine position. It is possible that the resultant error is small; but its magnitude in a few cases may be signifi-

cant, and there is no way of suspecting in which cases the error is serious. For these reasons the elaborate technique does not appear to justify itself.

In the following statement Jacobs¹⁰ does not mention the focus-film distance, nor does he at any time state the distance he uses: "experimenting with the bony pelvis, I have shown that discrepancy of only 5 degrees between the inlet and film produces an error of 0.5 cm.; an error as great as 1 cm. could easily be encountered." If such a statement were harmless as well as meaningless one would disregard it; but it may mislead the uninitiated!

There is an impression that Ball^{29, 30} has reduced the degree of disproportion between head and pelvis to simple mathematical terms. Ball chooses a pelvic diameter and replaces the figure by the volume of the sphere having a diameter of the same length. A similar volume for the foetal head is calculated, and it is considered that this should not exceed the "pelvic volume" for a particular level by more than 150 c.c. If so, the disproportion is dangerous. If this concept is compared with the consideration of the area of a pelvic plane and the area of a cross-section of the foetal head, the former must surely be declared to be inferior.

SUMMARY AND CONCLUSIONS.

1. The value of X-ray pelvimetry is considered and simplicity in technique advocated. There are two objectives: the first is to reach a decision about the salient features of a pelvis which will give both its capacity and type; the second is concerned with the limitations of radiography in providing these desiderata, and can only be fulfilled by experiment showing the degree of precision of certain technical methods.

The conclusion reached is that, at the present, X-ray pelvimetry is precarious,

but that with simplified technique we may attain to results of such value that every primigravida should be radiographed.

2. Dioptrographic tracings were made of the pelvic brim and the outlet plane of least pelvic diameter of a collection of skeletal material. The outlines were considered as ellipses, their areas found with a planimeter, and compared with the calculated area. In the case of the brim a mean error of -8.5 per cent was thought to be too great, and a modification introduced which gave an error limit of less than 5.0 per cent. For the outlet, the calculated area may show an error up to 10.0 per cent, but it is shown how this error may be reduced.

3. A new method of obtaining the distance between the ischial spines is shown. The error is less than 1 per cent, which amounts to being less than 1 mm. With the pelvic brim horizontal, the ischial spines are in all cases very close to 3.0 cm. from the table surface, and this makes the calculation possible.

The pubosacral diameter cannot be measured precisely on a lateral view film, because the anterior point is indeterminate. Even by Nicholson's stereometric method the posterior point inaccuracy is too great to warrant the expense and trouble of exposing a film for this diameter only. Clinical measurement is at least as accurate, and figures are given to show what subtraction for the sacral thickness is necessary in this case.

4. The level of the spine of the last lumbar vertebra, relative to the pelvic brim and promontory, is discussed fully. With the brim horizontal, the last lumbar spine is at the level of the conjugata vera. It is shown how lordosis aids in producing a horizontal true conjugate with a semi-recumbent position convenient for X-ray work.

5. An antero-posterior view in the above position provides the areas of inlet and

outlet, and an inlet index. No more than this is required for practical purposes except to palpate the pubic arch for height, width, and the height of the symphysis pubis. If the arch is suspiciously narrow, a radiograph giving accurate measurements can be obtained simply. It is considered that a lateral view of the pelvis is very rarely of value.

6. Unsatisfactory results with the transverse diameter of the brim led to experiments which show that by no X-ray method can the actual transverse of the brim be shown. This inlet seen on the skiagram represents a level near to that of the pelvic cavity. The iliac portion of the *iliopectineal line cannot be seen on any film*, and its anterior portion is usually simulated by other anatomical features. It is, therefore, impossible by radiographic means to obtain measurements of the superior strait, i.e., excluding the conjugata vera on the lateral film. The estimation of the area and the pelvic brim index for this level is discussed, and a solution offered.

7. A survey is made of the achievement of different X-ray methods of studying the obstetric pelvis. The conclusion remains, that our method of making only one exposure for the average case gives as much information for practical and clinical purposes as can at present be expected from radiography.

I have pleasure in acknowledging my thanks to the honorary radiologists of the Johannesburg General Hospital for the facilities allowed me, and their interest in my work; and to Miss E. Brown, chief radiographer at the non-European X-ray Department, and her staff for their patience in carrying out my radiographic work.

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growth showed a carcinoma of a similar structure. Sections from the liver and the vertebra also showed secondary carcinoma.

The examination suggested that in this case the primary growth was in the large intestine.

These 2 cases, one undoubtedly a primary ovarian carcinoma, were both given testosterone propionate; in the first case in fairly massive dosage. The immediate effect in both was to give the patients a feeling of well being, but this was only temporary and there was no evidence of any retrogression in the growth itself or the

metastatic deposits, either clinically or histologically.

In the *American Journal of Obstetrics and Gynecology* (December 1943), C. T. Beecham reports on 6 cases of ovarian carcinoma treated with testosterone propionate with somewhat corresponding findings.

But for the heavy cost of the testosterone propionate it might be well to try its effect on an advanced carcinoma of the uterine endometrium, as being the end organ on which the gonadic hormones act and therefore more likely to be influenced.

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Note of a Case of Extrophy of the Bladder with Procidencia

BY

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Surgeon, Leatherhead E.M.S. Hospital.

THIS case is recorded for two reasons. I can find only 2 other cases of ectopia vesicae with procidentia in the literature, though it would be reasonable to expect prolapse to occur fairly often in patients with wide pubic separation, and if attention is drawn to the possibility other cases may be recorded. Secondly, the combination does present a difficult problem, and a note of present experience may assist other surgeons.

The patient was aged 31, and was first admitted to Leatherhead E.M.S. Hospital in October 1939. She had already endured much surgery; before 5 years of age she had 8 operations in the Hospital for Sick Children, Great Ormond Street, and although the notes are not now available, it is believed that both ureters were transplanted into the bowel and attempts were made to close the abdominal wall. When she was aged 25 she was first seen at King's College Hospital by Mr. J. G. Yates-Bell, and I am indebted to him for the following information. When he first saw her there was a large cavity in the suprapubic area, lined by reddish mucosa. A fistula between this cavity and the sigmoid colon was demonstrated, and both faeces and urine (via the transplanted ureters) escaped through the cavity, and also through the rectum. In successive stages the ureteric anastomoses were refashioned in fresh bowel (further from the fistula) and the fistula closed, the parietes being drawn together as far as possible. A final granulating area was covered by pinch grafts.

As is usual in these cases, the pubic rami and labia were widely separated, and the position of the symphysis and *mons veneris* was occupied by a narrow bridge of skin and fibrous tissue. The perineum was normal. At times the cervix protruded just outside the vaginal orifice, and the anterior vaginal wall was everted below this bridge of skin. The prolapse was controlled by a cup and stem pessary. In 1936 right renal calculi were removed by pyelolithotomy, but further renal infection with poor function on that side necessitated nephrectomy in March 1939.

When the patient came under my care in October 1939 she was complaining of severe discomfort due to her prolapse. Her general condition was good, with a blood-pressure of 126/90 mm. and a blood-urea of 37 mg. per 100 c.c. Her urine could not be examined as it was discharged rectally, but her temperature chart did not show any evidence of further renal infection and intravenous pyelography showed a normal left kidney with good excretion. She could hold her urine rectally for 2 hours.

By this time the prolapse was complete, and the whole vagina was everted, with severe infection and crusting over the mucosa. The local inflammation was so severe that she could not use her cup and stem pessary, and could not walk or sit in comfort. Her periods were regular and normal, but she found menstrual hygiene most difficult. She refused to consider any further use of a pessary and gladly con-

sented to an attempt at surgical cure, though success could hardly be promised.

It was felt that vaginal hysterectomy and repair would have many advantages over less radical procedures, as pregnancy would be a grave danger to her renal health, and it was hoped that the stretched cardinal ligaments could be more effectively sutured after removal of the uterus. In the absence of the normal fascial layers of the anterior vaginal wall, the whole success of any repair would depend on these ligaments. Interposition was not feasible; le Fort's operation was undesirable at her age; and any intra-abdominal fixation was impossible as the lower abdominal wall was only represented by an attenuated scar. There was one real risk—injury to the one remaining ureter—the precise point of entry of the transplanted ureter being unknown.

After some days of local preparation, operation was performed under gas, oxygen and ether anaesthesia. The posterior fornix was first incised and the pouch of Douglas sought. It was obliterated by adhesions, but the posterior wall of the uterus was fairly easily followed by gentle dissection, the distended rectum being pushed backwards, and freed with a little more difficulty from the fundus of the uterus, where rather denser adhesions were encountered. The "Fothergill incision" was next made down the anterior vaginal wall and around the cervix, and the anterior wall of the uterus dissected free from a mass of fibrous tissue that occupied the normal place of the bladder. When the fingers met over the fundus of the uterus, the broad ligaments were defined and clamped in the usual way, and the uterus removed. It was interesting to observe that the supravaginal part of the cervix was elongated just as in the ordinary case of prolapse. The broad ligaments were sewn together, and the usual anterior wall repair

done. In view of the gross local sepsis and some fear for the vitality of the rectal wall after its separation from the uterine adhesions, a little packing was placed in the posterior fornix, which was not completely sutured, but left to granulate. A rectal tube was passed to drain urine freely from the bowel and prevent distention.

Recovery was uneventful. So far as the position of the fornix was concerned the immediate result was good, but it must be admitted that there was still some bulging of the anterior wall, where the normal pubo-cervical supports were deficient. The mucosa soon recovered its normal moist surface and pliable consistence, and the local infection subsided. The patient was delighted with the result and in 1942 wrote to tell me that she had married, and when I saw her did, indeed, seem a different individual. In 1943 she was seen again and, as it was feared that the anterior wall bulge was increasing, she was given a modified ball and stem pessary, which she was able to wear with comfort. If in the future this eversion still progresses then there will be no alternative but to perform some type of le Fort procedure.

The only record of a similar case¹ that I can find was that of a Sudanese woman, aged 25, and in that case transplantation of the ureters was the only treatment, and there was no attempt to deal with the prolapse. One other case of *ectopia vesicae* complicated by *procidentia* was reported by Bonnet² as long ago as 1723, but in that case the prolapse followed the free division of the perineal body to complete a difficult delivery, and the brief account does not mention treatment. Several cases of pregnancy in patients with extrophy of the bladder have now been reported, and it would be interesting to know if any of these subsequently developed prolapse.

In the present case complete success in treatment of the prolapse cannot be

claimed, but enough was achieved to allow the patient to marry, and to rid herself of that feeling of inferiority that so often goes with gross developmental abnormalities. Her ultimate prognosis depends on the fate of her remaining kidney, and a few recent attacks of pain in the loin with fever suggest that some ascending infection must be feared. The photograph (Fig. 1) shows the result, with the wide pubic separation,

the abdominal scar, and the bulging anterior vaginal wall.

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FIG 1

Showing postoperative result Note the wide separation
of the pubes, the abdominal scar and the bulging anterior
vaginal wall

S G C

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Extragenital Chorionepithelioma

Report of a Case with Chorionepithelioma of the Breast occurring during the Course of Pregnancy.

BY

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A STUDY of the literature on chorionepithelioma shows that two main varieties of this rare condition exist.

The first, which is known as Genital Chorionepithelioma, is the more common type described in all modern textbooks of gynaecology. As the name suggests, the genital tract is primarily involved by the growth, secondary deposits manifesting themselves in the lungs, liver, brain, and other organs.

This group may be further subdivided into two varieties depending on the site of origin of the neoplasm.

(1) *Uterine chorionepithelioma*, first described by Sanger¹ in 1889 as deciduoma malignum, and now generally recognized as the commonest site of origin of this type of malignant growth.

(2) *Extrauterine chorionepithelioma*, characterized by the presence of a neoplasm in the genital tract without any microscopic evidence of its presence in the uterus. The commonest site of these growths is the vagina, and has been described by Zagorjanski-Kissel,² Findley,³ and others, as primary vaginal chorionepitheliomata. Dougal⁴ and others have described the occurrence of primary ovarian chorionepitheliomata and Cope and Kettle⁵ the presence of primary growths in the Fallopian tubes.

The second main variety, which I propose to deal with in this paper, is the Extragenital Chorionepithelioma, in which

chorionepitheliomatous growths have been found in other organs of the body, remote from, and without any evidence of a similar growth in, the genital tract. Dunger⁶ spoke of such instances as examples of "ectopic" chorionepithelioma.

LITERATURE.

Although genital chorionepithelioma is often described in the English literature, I have been unable to trace any recorded case of the extragenital variety except in the American and Continental records.

The first recorded case of extragenital chorionepithelioma was described in 1900 by Davis and Harris,⁷ in a woman aged 40 years who had been pregnant 14 times. Her youngest child was 14 months old. She was admitted to hospital in extreme prostration with a history of 2 months' amenorrhoea. Describing the case in their own words—"early pregnancy was diagnosed. No improvement in her general condition occurred and the uterus was dilated and emptied under ether. She, however, did not regain strength, had paroxysmal attacks of vomiting, became at times maniacal, passed urine and faeces involuntarily and died of apparent exhaustion. A probable diagnosis of temporary insanity, of malnutrition and anaemia was made." Autopsy revealed 9 irregular tumour-like masses in the brain, with similar growths in the lungs, left kidney, liver and thyroid gland. The uterus appeared

to be normal. Microscopic examination showed the growth to be a typical chorionepithelioma.

Marchand⁸ in 1898 described a case in which neoplastic foci of chorionepithelioma were found in the brain, lungs, and kidney 1 month after removal of a hydatidiform mole from the uterus. No evidence of a primary tumour was discovered in the genitalia. The uterus was found to be "somewhat enlarged and there was decided decidual formation *in utero*."

In 1902, Senarclous⁹ reported the case of a woman aged 38 years who had had 1 child. In 1898 she had an early abortion and in November 1901 there appeared a foul smelling bloody discharge from the vagina, together with severe abdominal pains. In February 1902, i.e. 4 years after gestation, an abdominal tumour was recognized and diagnosed as "a swelling in the right adnexa." Death occurred 1 month later, shortly after abdominal section. Postmortem revealed multiple growths in the lungs, anterior mediastinum, wall of the right ventricle of the heart, thyroid gland, suprarenals, and kidneys. Microscopic evidence of an atypical chorionepithelioma was found in all the above organs. The Fallopian tubes, ovaries and uterus were normal.

In the same year, Busse¹⁰ quoted the case of a patient aged 40 years who entered hospital with a right-sided hemiplegia and who died soon afterwards. Autopsy showed extensive chorionepithelioma of the lungs, liver, kidneys, pia mater, and intestines. The primary growth was not recognized, but the genitalia were not involved.

Fischer¹¹ in 1913 described the case of a woman aged 45 years, who had had 2 deliveries, the last 18 months prior to admission to hospital. Necropsy disclosed numerous nodules in the liver, varying from 2 to 6 cm. in diameter. There was invasion of the hepatic veins by chorion-

epitheliomatous growth. The head of the pancreas revealed a similar nodular neoplasm. Microscopy revealed a typical chorionepithelioma. The uterus on examination was normal.

Gurewitsch¹² in the same year, described chorionepitheliomatous growths in the liver, intestine, lungs, and mesentery of a patient aged 31 years, 18 months after a hydatidiform mole. Although the uterus showed decidual changes, no evidence of a neoplasm was found. The ovaries contained lutein cysts.

Christeller and Oppenheimer¹³ described an interesting case in 1925, of a patient aged 52 years who died 12 years after a pregnancy. Chorionepitheliomatous deposits were found in the liver, lungs, and intestine.

Nolasco,¹⁴ in 1927, found neoplastic deposits of chorionepithelioma in the lungs, liver, and kidneys of a patient in whom no genital involvement could be found.

In Budapest in 1928, De Zalka¹⁵ reported a similar case to that described by the previous authors. The patient, aged 46 years, whose menses started at the age of 15 years, continued to menstruate regularly up to 35 years, at which time her periods stopped. She had had 5 pregnancies and 2 of her children were alive and well. In February 1920 she observed a small tumour in the right abdominal region, which about 10 months later occupied the entire right abdomen. In January 1921 the patient entered hospital and a large mass, presumably liver, was found extending 8 cm. below the costal margin. Her genitalia, although showing atrophy, were normal. A diagnosis of multiple liver gummata was made, because of a strongly positive blood Wasserman reaction and the presence of "luteic scars" on the lower limbs. The patient became cachectic and the nodular hepatic tumour increased in size. She died 1 month later. At autopsy

chorionepitheliomatous nodules were found in lungs, liver, and kidneys. De Zalka believed that the tumour in the liver was primary as it was the largest tumour, and the uterus did not contain a tumour.

Novak and Koff¹⁶ in 1936 reported the case of a woman aged 31 years, who was admitted to hospital because of headaches and failing vision of several months' duration. Seven months previously vaginal bleeding began. Curettage was performed 2 months later and revealed normal retained products of conception, later confirmed by microscopic section. Death occurred 5 months later and chorionepitheliomatous growths were discovered in the left occipital lobe, lungs, and kidneys. Histological examination of the uterus did not reveal any abnormality.

In 1931, Lapointe, Cain, and Darfeuil¹⁷ found chorionepitheliomatous deposits in the small and large intestines of a woman aged 32 years who died 3 years after abortion.

Four years later Bonne¹⁸ published a case of chorionepithelioma which exhibited foci in the lungs and brain of a woman aged 30 years. A history of pregnancy was not mentioned.

Gerber¹⁹ in the same year, 1935, quoted a case similar to that of Bonne's. Again there was no history of pregnancy. The lungs showed deposits of chorionepithelioma with no foci in the genital tract.

Berman²⁰ in 1940 described a case of a woman aged 39 years, who gave a history of pregnancy 14 months before. Autopsy revealed chorionepitheliomatous masses in the liver, lungs, spleen, intestine, and brain.

The last reported case was by Maun and Green²¹ in 1943, who recorded a case in a primigravida who was delivered normally of an infant on May 28th, 1942. The placenta was expelled spontaneously but was not submitted for laboratory investigation.

Three months later she was admitted to hospital complaining of progressive weakness and chills of 2 weeks' duration. Except for anaemia, which was treated with iron therapy, nothing abnormal was detected and she was discharged in September 1942. Eleven days later she was again admitted with increasing weakness and she died on the 25th September 1942, i.e. 5 months after confinement. Postmortem revealed a large tumour in the liver which on microscopic examination showed a typical chorionepithelioma. The lungs were normal and no evidence of a genital neoplasm was discovered, although multiple sections of the uterus were investigated.

To the above 15 cases of extragenital chorionepithelioma I would like to add a sixteenth, the extreme rarity of which is sufficient to justify its publication, as not only are there no recorded cases of such a condition in the literature of this country, but also no reference to the extragenital type of growth is made in the British textbooks of Gynaecology.

CASE HISTORY.

Mrs. L. B., a married woman, aged 27 years, was admitted to this hospital on June 10th, 1944, as an emergency, complaining of absence of foetal movements of 1 week's duration and a lump in her right breast which had first appeared 2 months previously.

The history obtained was that in 1940 she had had a normal delivery of a living child, and in March 1943, a 14 weeks abortion. Since then her periods had been regular and normal until early November 1943 when her last menstruation was stated to have occurred.

She had been attending an antenatal clinic and was well until 2 months before admission to hospital, when she first noticed a small lump in the right breast, which had gradually increased in size. She did not complain of any pain or tenderness in the swelling and no unusual discharge had been noticed from the nipple.

About 1 week before admission to hospital she detected the absence of foetal movements, which had been present every day since the 20th week of her pregnancy. At about the same time she complained of increasing listlessness and shortness of breath with the slightest exertion. She called in her doctor, who sent her to hospital.

Examination.

The patient had a sallow complexion and there was distinct pallor of the mucous membranes. Temperature, 98.6°F.; pulse-rate, 110; respiration-rate, 20; blood-pressure, 138/90; urine, clear; heart-rate 110 per minute, regular. Soft apical systolic murmur heard over the mitral area; lungs, clear.

Right breast. An obvious enlargement was noticeable, due to a lump in the median lower quadrant. No signs of inflammation were present. On palpation a non-tender, smooth, and freely mobile swelling, the size of a billiard ball, was felt in the median lower quadrant of the breast. There was no attachment to the skin, nipple, or deeper structures. No axillary glands were felt.

A provisional diagnosis of fibroadenoma was made. Surgical intervention was not deemed necessary until after termination of the pregnancy.

Abdomen. Height of the fundus uteri equivalent to a 32 weeks pregnancy. Vertex presentation palpated. Foetal heart sounds were not heard.

A diagnosis of intrauterine death was confirmed by X-ray examination.

June 13th, 1944. Blood examination: haemoglobin, 45 per cent; red-blood corpuscles, 2,400,000; colour index, 0.9.

Two pints of blood were administered.

June 14th, 1944. Medical induction. Benztrone 100,000 I.B.U. b.d. for 2 days followed by oil, enema, and pitocin. Unsuccessful.

June 17th, 1944. Similar induction to the above repeated with the same result.

June 18th, 1944. High puncture of the membranes performed, and 18 ounces of meconium-stained liquor drained off. Five hours later delivery of a macerated stillborn child occurred, followed soon afterwards by a very unhealthy-looking placenta which was not submitted for laboratory examination. Postpartum loss was normal. Following delivery, the general condition of the patient deteriorated, the pulse-rate varying

between 120 and 140 with marked pallor. In spite of repeated blood transfusions (about 9 pints were administered over a period of 13 days) increasing cachexia occurred. Death took place on July 1st, that is, about 2 weeks after delivery.

Repeated blood cultures and a cervical smear were negative. Vaginal examination performed on June 23rd revealed slight tenderness in the left fornix. The only other feature of note, which occurred on June 21st, was a very profuse offensive non-blood-stained lochia.

Postmortem Findings.

Fairly well-nourished adult female.

Right breast. A swelling 4 inches by 2 inches by 1½ inches in size was excised from the substance of the right breast in the median and lower quadrant (Fig. 1). Sharply demarcated from the normal breast tissue, the lump was of a greyish mottled appearance with several haemorrhagic areas. Necrotic and friable in consistence.

Microscopic appearance. (Figs. 2, 3 and 4.) The tumour consists mainly of necrotic tissue with marked areas of haemorrhage. The central portion is made up of fibrin and red-blood cells. Trophoblastic cells are present around the periphery of the tumour showing marked pleomorphism. Langhans' and syncytial cells are present. The area of necrosis is out of all proportion to the small number of malignant cells found.

The appearance of the tumour is that of a typical chorionepithelioma.

Uterus. Size 7½ inches by 5 inches by 4½ inches (Fig. 5). Placental site identified in the right anterior wall of the fundus. Evidence of any form of neoplasm was not discovered.

Microscopy. Sections cut from the wall of the uterus failed to show any abnormality.

Ovaries (Fig. 5). Both ovaries were enlarged, 3 inches by 2½ inches by 1½ inches, and cystic. On section multiple cysts were found, filled with amber coloured fluid.

Microscopic appearance. Multiple cysts of the paralutein variety present. Evidence of malignancy was not found.

Lungs (Fig. 6). Almost the entire surface of both lungs were studded by multiple purplish blue nodules, raised above the surface of the normal lung substance. The nodules, which varied in size from about ½ inch to 3 inches in diameter, are of

solid consistence. Cross section of the tumours disclosed necrotic friable masses of haemorrhagic tissue, well demarcated from the surrounding lung.

Microscopic appearance. The tumours consisted mainly of necrotic foci of tissue with well-marked areas of haemorrhage. Large numbers of syncytial and Langhans' cells were present.

Liver. As in the lungs this organ was enlarged and studded with multiple nodules varying in size from 1 inch to 1½ inches in diameter. The appearance is similar to the above organs microscopically.

Spleen, kidneys, and suprarenals showed similar appearance to the organs described above. The brain was not examined.

Conclusion. Extensive chorionepithelioma of the extragenital type.

DISCUSSION.

Several aspects of the present case seem worthy of discussion and comparison with the cases recorded above.

Relation to Pregnancy.

In respect of its clinical relation to pregnancy, three types of chorionepithelioma may be distinguished (Teacher,²²).

1. That in which the disease develops during pregnancy.

Many cases of genital chorionepithelioma falling into this group, have been reported. The commonest site described appears to have been the vagina. Out of the 16 cases of the extragenital variety reported above, the only case which appears to have developed during the course of pregnancy, is the one described in the present paper. The occurrence of a chorionepithelioma of the extragenital variety during pregnancy was emphasized by the appearance of a neoplastic focus in the right breast 11 weeks before death. One cannot of course exclude the 14 weeks abortion, which had occurred 8 months previously, as the original basis for the development of the growth, in which case one could include the case described as being both postpartum and intrapartum.

2. That in which the disease develops after a definite interval of several months to several years.

The vast majority of cases of both genital and extragenital variety fall into this group.

3. That in which the clinical relation to pregnancy is obscure.

In this group one can include the cases of so-called "teratomatous" origin (*vide infra*).

Nature of the Pregnancy Immediately Preceding the Occurrence of the Chorionepithelioma.

Teacher²² in a series of 188 cases of all types reported the following:

| | Cases | Per cent |
|----------------------------------|-------|----------|
| 1. After hydatidiform mole | 73 | 36.6 |
| 2. After abortion | 59 | 31 |
| 3. After labour at or about term | 49 | 28 |
| 4. After extrauterine gestation | 7 | 4.4 |

Dorland²³ in a series of 50 cases found the following:

| | Cases | Per cent |
|----------------------------------|-------|----------|
| 1. After hydatidiform mole | 20 | 40 |
| 2. After labour at or about term | 17 | 34 |
| 3. After abortion | 12 | 24 |
| 4. After tubal pregnancy ... | 1 | 2 |

In the 16 cases of the extragenital variety reviewed above:

1. Five cases occurred after labour at or about term (31.25 per cent).
2. Four cases occurred after abortion (25 per cent).
3. Two cases occurred after hydatidiform mole (12.5 per cent).
4. Four cases gave no history of pregnancy (25 per cent).
5. One case occurred during the course of pregnancy (6.25 per cent).

Distribution of the Tumours.

In the 16 cases reported, the distribution was as follows:

Thirteen in the lungs, 10 in the liver, 8 in the kidneys, 7 in the intestines, 5 in the brain, 2 in the suprarenals, spleen and



FIG. 1.
CHORIONEPITHELIOMA OF THE BREAST

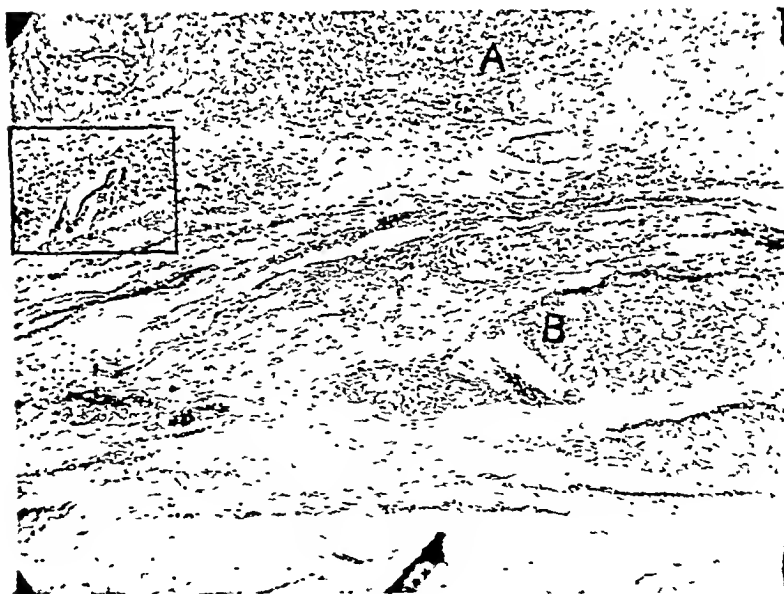


FIG. 2.
CHORIONEPITHELIOMA OF THE BREAST
A. Area of haemorrhage and necrosis
B. Normal breast tissue
Squared area—Chorionepithelioma

L. R.

× 50



FIG. 3.
CHORIONEPITHELIOMA OF THE BREAST.
Squared area of Fig. 2 under high power. × 120

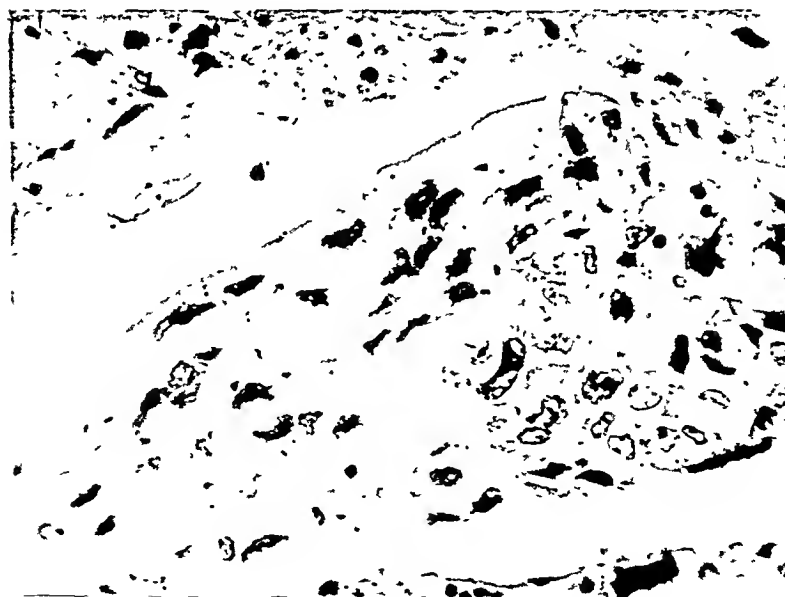


FIG. 4.
CHORIONEPITHELIOMA OF THE BREAST.
High-power view of squared area. Note syncytial and
Langhans' cells.



FIG 6

CHORIOEPITHELIOMA OF THE LUNGS



FIG 5

UTERUS AND OVARIES

Placental site in anterior aspect of fundus Note bilateral multiple theca lutein cysts of ovaries

L R

thyroid, one each in the mediastinum, heart, pancreas, and breast.

It is noteworthy that out of the 16 cases, in 13 the tumours were found in the lungs, and in 10 in the liver, which seems to suggest that these two sites are the commonest for the development of extragenital chorionepithelioma. The occurrence of chorionepithelioma in breast tissue in the case recorded in the present paper, is particularly interesting, as not only is this the first recorded case but also this feature was the deciding factor in concluding that the chorionepithelioma occurred during the course of the pregnancy.

AETIOLOGY.

The occurrence of chorionepitheliomatous growths in extragenital organs without microscopic evidence of a primary focus in the genital tract, has led to the formulation of several theories regarding the origin of the tumours.

- (1) *Transportation of chorionepitheliomatous emboli from a previous chorionepitheliomatous placenta completely expelled during labour.*

Schmorl²⁴ examined the lungs of 158 patients dying at different stages of pregnancy or after delivery and found chorionic cells in the lung capillaries in 80 per cent of the normal pregnancies. In the lungs of women dying of eclampsia, chorionic cells obstructed the capillaries, sometimes extensively, in every case examined. In 8 out of 22 cases dying of abortion, during the first 2 months, there were chorionic cells in the lung capillaries. In only 3 cases was there evidence in the lung capillaries of chorionic cell proliferation, and in view of the lack of examination of the placenta, hydatidiform or chorionepitheliomatous changes could not be excluded.

In accordance with these findings,

Schmorl laid emphasis on the possibility that "ectopic" chorionepithelioma might originate from a previous mole, or chorionepitheliomatous proliferation of a placenta completely expelled during labour. He quoted a case in which 18 weeks after a normal pregnancy, a tumour was detected in the vagina. Death occurred within 6 months. The uterus and appendages were not involved by any growth, but metastases were found in the lungs, liver, kidney, and intestines. The vaginal neoplasm and the metastases gave the typical picture of a "syncytial" growth.

Schmorl believed that the process had originally started in the placenta which, however, had been expelled before the uterus was directly attacked, but not until metastases had commenced.

- (2) *Malignant transformation of transported chorionic emboli from a normal placenta.*

Marchand⁸ and Pick²⁵ maintained that chorionic cells or villi deposited during normal pregnancy may likewise give rise to chorionepithelioma, and that most cases of "ectopic" chorionepithelioma revealed a history of normal pregnancy, hydatidiform mole being relatively rare.

The opinions of Marchand and Pick received support from an observation made by Walthard²⁷. He found a chorionepitheliomatous nodule in the vaginal wall of a patient during the 8th month of her 5th pregnancy. Caesarean section and total hysterectomy were performed and evidence of either a mole or neoplasm was not found in the uterus or placenta. Death occurred 7 months later, chorionepithelioma being found in the liver, lungs, and left kidney. The author considered the nodules to be metastases from a primary "ectopic" chorionepithelioma of the vagina, developed during the course of a normal pregnancy.

- (3) *Complete regression of the uterine tumour with continued growth of the metastases in distant organs* (Novak²⁸).

Cases of spontaneous cure or cure after incomplete operation have been described by several authors including Neuman,²⁹ Pick,³⁰ and Teacher.²²

Novak²⁸ considers that approximately 10 per cent of cases undergo such a favourable course.

Kelly and Teacher³¹ demonstrated histologically that some of the tumours in the parametrial veins had become extinct, the tumour cells being embedded in thrombus, the formation of which apparently destroyed them.

In 1907 Teacher was able to demonstrate healed nodules in a case of chorionepithelioma and to give some account of the healing process.

The view that the spontaneous cure resulted from shutting off of the blood supply of the tumour through choking of the blood vessels by trophoblastic tissue has been abandoned (Novak). The more probable explanation appears to lie in some unknown factor of general body resistance to the inroads of the disease.

The same explanation would seem to hold good for cases in which primary uterine tumours were found to be present, with distant metastases such as in the lung, and yet healing has occurred without radical operation (Pick,³⁰ Neuman²⁹).

- (4) *Chorionepithelioma developing from the trophoblast of an extragenital teratoma.*

This possible explanation was first recognized by Kanthack and Eden,³² and demonstrated to the London Obstetrical Society in 1896 in connexion with the discussion on deciduoma malignum, when it was recognized that malignant tumours identical with chorionepithelioma have

been observed apart from pregnancy, and even in men.

Schlagenhauser³³ advanced the view that the primary growth was a mixed tumour or teratoma, and that the chorionepithelioma-like tissues represented the chorionic epithelium. Many of these cases are described for the most part in connexion with the testes.

Lubarsch³⁴ described a chorionepithelioma occurring in a girl 13 years of age, who had never menstruated. In this case, the tumour was found to be attached to the uterus.

Ritchie,³⁵ in 1903, found a chorionepithelioma which had occurred in a dermoid of the mediastinum of a man, and which had given rise to extensive metastases.

Emrys-Roberts and Walker Hall³⁶ in 1910, found a tumour in the retroperitoneal space between the kidneys of a man. Section of the growth disclosed a typical chorionepithelioma.

Suggested Cause for the Extragenital Tumours in the Present Case.

In relation to the present case, an explanation for the aetiology can be sought for in the theories outlined.

Bearing in mind that trophoblast is a normally invasive tissue and that masses of normal trophoblastic tissue and even clumps of chorionic villi may be deposited in distant fields, particularly the lungs, one cannot exclude the possibility of a chorionepitheliomatous transformation of such tissue in the lungs and the consequent extensive spread.

Considering Schmorl's³⁴ view of the transportation of chorionepithelioma emboli from a prior chorionepithelioma placenta, complete abortion, or during labour, it is not unlikely that such events may have

the deposit of malignant foci in the lungs, primarily, as this organ is most commonly affected. Hence the explanation for the extensive secondary spread including the breast.

One could regard the theory of complete regression of a primary tumour in the uterus as unlikely in the present case, in view of the short period elapsing between expulsion of the placenta and the death of the patient, i.e., 13 days.

The theory of a teratomatous basis for the development of the chorionepithelioma is also unlikely in this case, in the presence of a 32 weeks pregnancy.

One might therefore conclude that in the present case the explanation for the development of the extragenital chorionepithelioma is a matter for conjecture. The cause can be sought for in the first two theories outlined. The chance that chorionepitheliomatous elements were present in the uterus, but in such minute quantities that they were overlooked, even after a most careful investigation of the entire genital tract, is also within the realms of possibility.

SUMMARY.

(1) Chorionepithelioma has been classified into two main groups:—

(a) *Genital group*, further subdivided into (i) *Uterine*, and (ii) *Extrauterine varieties*, i.e., primary vaginal, ovarian, and Fallopian tubes.

(b) *Extragenital group*, defined as chorionepithelioma manifesting itself in organs of the body remote from, and without any microscopic evidence of a similar growth in, the genital tract.

This group is dealt with mainly in this paper.

(2) The literature of 15 reported cases of extragenital chorionepithelioma is reviewed.

(3) The description of another case is given.

The case recorded is of particular interest, in that such a recorded case of extragenital chorionepithelioma has never appeared in the literature of this country, and manifesting a breast chorionepithelioma.

(4) A short discussion of its relation to pregnancy, the nature of the pregnancy immediately preceding the occurrence of chorionepithelioma and the distribution of the tumours is outlined.

(5) The aetiology of extragenital chorionepithelioma is briefly outlined, and an explanation for the origin of the growths occurring in the present case is offered.

My thanks are due to Mr. George Brown, Medical Superintendent to this hospital, for his permission to publish this case, and to Professor Daniel Dougal for his kind advice and criticism. For the clinical photographs I am indebted to Sister Winters.

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A Case of Coexisting Tuberculosis and Cancer of the Uterus

BY

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THE simultaneous occurrence of tuberculosis and cancer has been reported as being infrequent. The first observation is credited to Rokitsky,¹ who stated that the two processes occur together rarely, and that this is even more true of the two processes in the same organ. This statement has been repeatedly substantiated by others, including McCaskey² and White.³ Nevertheless observations have been made and recorded concerning the occurrence in the same organ, but much more rarely than in the same organism. Until 1908 only 9 cases of carcinoma of the uterus with co-existing tuberculosis had been reported (Veit⁴), and they mostly showed squamous epithelioma of the cervix with tuberculous endometritis, or peritoneal tuberculosis as distinct from uterine disease. Comprehensive reviews by Wallart⁵ and von Franqué⁶ are the more exhaustive of the older literature.

Gais⁷ reviews 27 cases of simultaneously occurring carcinoma and tuberculosis of the uterus and adds the description of his own case.

The earlier cases were thought to show that tuberculous endometritis was an aetiological factor in the production of the neoplasm, and that the malignant change occurred in the already diseased tissue as a result of chronic irritation, but most writers to-day rather believe that carcinoma and tuberculosis together are merely coincidental and have no bearing on one another except that carcinoma may predis-

pose to secondary tuberculous involvement of the organ when a primary focus is present elsewhere in the body.⁷ More recently cases have been reported by Petridis,⁸ Novak and Windholz,⁹ Ravid and Scharfman.¹⁰ In view of the rarity of the association the following case is reported.

CASE HISTORY.

Mrs. R. R., aged 44, was admitted to a surgical ward in November 1943 complaining of pain in the right side. A diagnosis of acute appendicitis was made, the abdomen was opened, and a chronically inflamed appendix removed. During the operation it was found that the uterus was enlarged and both ovaries were small and atrophic. Evidence of tuberculosis was not then found. Progress was uneventful and the patient was later referred to the gynaecological department on November 24th, 1943. The gynaecological report stated "Uterus anterior, soft, globular and about the size of a grape fruit; ovaries not palpable." The patient had a history of a yellow vaginal discharge from January 1943 to August 1943, but this was relieved by pessaries given by her own doctor. The nature of the pessaries is not known. In December 1943 she was admitted for investigation. On December 1st, 1943, she experienced a sudden gush of thick yellow discharge from the vagina, followed by blood-stained fluid, preceded by, and followed by, severe abdominal pain. Examination revealed extreme tenderness

above the pubic symphysis and a mass was palpable through the anterior fornix.

Examination under anaesthetic.

The uterus was now retroverted and slightly enlarged anteriorly, but smaller than on November 24th, 1943. Curettings were not obtainable and uterine discharge was not present. Further treatment was not considered necessary. On March 30th, 1944, the patient was readmitted. She had been bleeding *per vaginam* for the previous 3 weeks and abdominal pain had become more severe. She now complained of frequency of micturition, and blood now came in large clots.

Vaginal examination.

The uterus was enlarged, retroverted, and a mass was palpable in the anterior fornix.

On April 7th, 1944, a subtotal hysterectomy was performed, with removal of the right adnexa. White nodules were present at the uterine end of both Fallopian tubes, and the ovaries appeared healthy. On opening the uterus a growth was seen in the posterior uterine wall, protruding into the cavity. The diagnosis of carcinoma of the body of the uterus was made, with metastatic deposits in both Fallopian tubes.

Macroscopic examination.

The uterus, which had been removed supravaginally, measured 10 by 8 by 5 cm. The right Fallopian tube and ovary were attached, and adjacent to the proximal end of the tube there was a soft whitish nodule, 1 cm. in diameter, with the appearance of tumour tissue. The right ovary was small, scarred and firm, measuring 2 by 1 by 0.5 cm. It presented no obvious gross abnormalities.

Arising from a broad base in the fundus of the uterus was a bulky, papillary, friable mass, whitish-grey in colour, projecting

into, and almost completely filling the uterine cavity. The base of the tumour was not well defined. Areas of necrosis were numerous, but caseation was not observed. Below the main tumour mass two small whitish circular nodules, 1 cm. and 1.2 cm. in diameter respectively, were present on the posterior wall, the first 1.5 cm. and the second 3.5 cm. below the main growth. These areas were slightly raised and appeared to be metastatic neoplastic processes, as if produced by lymphatic permeation. The myometrium was thickened and fibrosed, with prominent vessels visible, and measured 2.25 cm. in thickness. Definite tumour tissue or nodules were not seen in the interstitial tissue. The external surface of the uterus appeared normal. The left ovary and Fallopian tube were unattached.

Microscopic examination.

Representative blocks, fixed in saturated mercuric chloride with 10 per cent formalin and embedded in paraffin, were examined. The structure of the tumour mass was that of a cellular anaplastic growth in which were a few cystic spaces containing pinkish hyaline material. The cells were mainly large and clear with large vesicular nuclei, many being vacuolated, and arranged in alveoli; mitotic figures were numerous. The stroma was thin and scanty, showing polymorphonuclear infiltration as well as some large mononuclear cells containing coarse brown pigment granules. The surface showed ulceration and necrosis with a layer of polymorphs and fibrin superimposed. Considerable areas of necrosis with hyalinization of the stroma and polymorphonuclear infiltration were present. An occasional gland-like space containing polymorphs and *débris* could be seen. Some areas of epithelium showed squamous metaplasia. Near the margin of the tumour, tubercle follicles

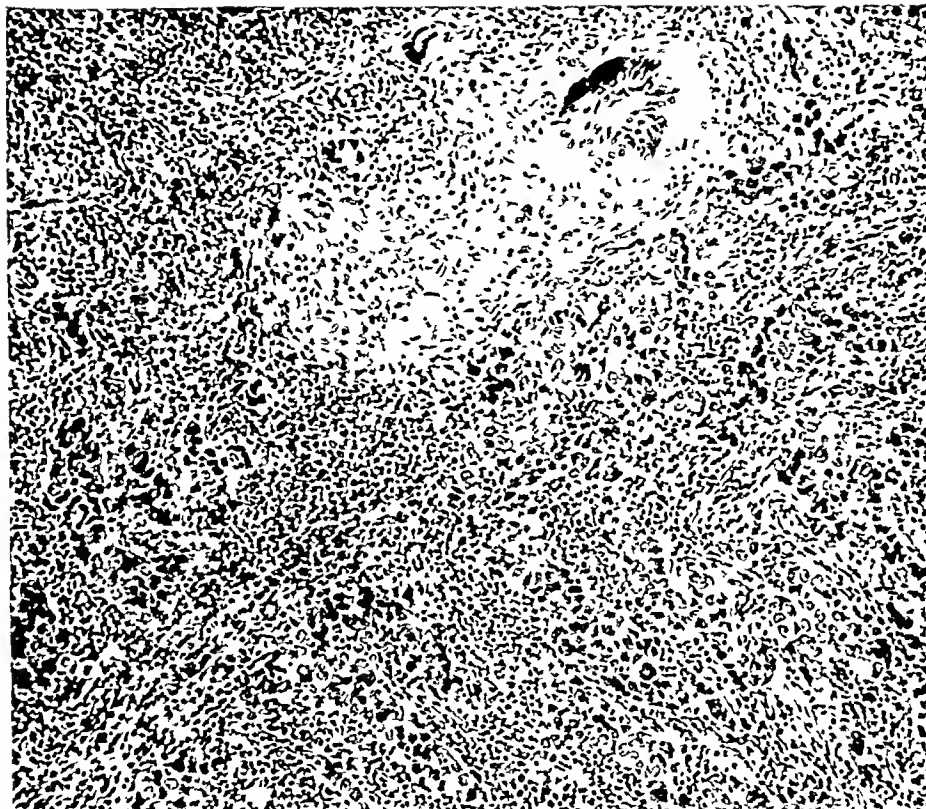


FIG 1.

Section from small nodule 1.5 cm below main growth. Note one tubercle follicle with giant cell, separated from tumour cells by zone of lymphocytes and fine connective tissue
 x 50 diameters. Stained Celestine Blue and Chromotrope

G H S

present. These follicles did not caseation, but consisted of central of necrosis surrounded by proliferating endotheloid cells with a peripheral leucocytic mantle and centrally placed cells. The endometrium beyond the outer margin was thin, with scanty glands, the epithelium of which, however, fairly high. The stroma of the endometrium was the seat of marked chronic inflammatory change but tubercle follicles were not present. Sections taken from the small nodules described above showed the same structure as the main tumour with the inclusion of tubercle follicles within the neoplastic process, near the surface. The nodules, mostly with giant cells, were separated from the tumour cells by a zone of lymphocytes and a layer of fine connective tissue. The endometrium beyond those nodules showed chronic inflammatory change with tubercle formation and small areas of caseous necrosis. In those sections the myometrium showed superficial penetration by numerous epithelial masses, while a few lymphatic channels contained clumps of tumour cells at some distance from the tumour mass. Other lymphatics frequently had aggregates of lymphocytes around them.

Transverse sections through the portion of the Fallopian tube first thought to be the site of metastasis revealed the nodule to be entirely made up of caseating tuberculous salpingitis with well-formed giant-cell systems. Tumour cells were not seen and evidence of peritoneal involvement was not present.

Sections of the right ovary showed hyaline degeneration of the walls of vessels and oophoritis. Corpora albicantia and areas of fibrosis were numerous.

Attempts to demonstrate tubercle bacilli in the lesions by the Ziehl-Neelson method were unsuccessful.

DISCUSSION.

The study of the tumour leads to the conclusion that it was an anaplastic adenocarcinoma of the body of the uterus. The tubercles were largely non-caseous and evidently fairly young. Their distribution and development would suggest that they are younger than the tumour and probably disseminated from the obviously older tubal lesion. It is interesting to find tubercle follicles in the tumour mass itself and in continuity with the neoplastic process. There is nothing to suggest that the tuberculous process has any bearing on the origin of the tumour. The cervix was not removed and unfortunately could not be examined. It appears, therefore, that the tuberculous involvement was secondary and probably by lymphatic or haematogenous spread from a distant focus, presumably the older tubal lesion. The association seems to be accidental, except that the uterine tumour may have acted as a favourable nidus for the development of the tuberculous lesion spreading from the Fallopian tubes.

The patient was investigated for further evidence of tuberculosis but neither pulmonary or renal lesions could be detected and she left the hospital in good condition. To date no further trouble has been reported.

SUMMARY.

A case of coexisting carcinoma and tuberculosis of the uterus is described, the former process apparently being the older one, the tuberculous lesion having probably been secondary to the tuberculous salpingitis.

I have to thank Dr. Jean Herring for permission to publish the clinical notes, and I am indebted to Professor D. F. Cappel for much helpful criticism and advice.

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Dysgerminoma of the Ovary in a Child of Five Years with Acute Torsion of the Pedicle

BY

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THIS case is reported on account of the comparative rarity of the tumour, the unusual clinical history, and because the girl in which it occurred was only 5 years of age, which is the youngest age I can find in the literature available.

In Novak and Gray's¹ paper on this type of tumour a total of 17 cases were reported, the youngest being 6 years of age. In one of these cases there was torsion of the pedicle.

The patient was a girl 5 years of age. On June 18th, 1943, she had a sudden attack of abdominal pain and 24 hours later was seen by a surgeon. She was vomiting, and was tender and rigid over the right iliac fossa. A large mass was also felt in this region on palpation and a diagnosis was made of a possible appendicular abscess and a laparotomy was performed. A tumour of the right ovary, which had twisted twice on its pedicle, was found and removed. No other abnormality was present, there were no abnormal sexual changes and the patient made an uneventful recovery.

Pathological report: "This tumour is the size and shape of a cricket ball and has a smooth, dense and intact capsule. On cutting it is white and brain-like in appearance and firm with a rubbery consistence. Cystic changes are not seen but oedema and congestion are present. The microscopic details are not all one would wish but this is due to the blood supply of the tumour having been obstructed for over

24 hours before removal. The main type of cell is large and round with abundant clear cytoplasm and a relatively large round or oval nucleus with a well-marked nuclear membrane and sometimes showing nucleoli. Occasional mitotic figures are seen. The cells are arranged in alveolar formations and in columns by fibrous septa which show hyalinization and contain many small lymphocytes and histiocytes. Two large symplasmic giant cells were found after an extensive search. This tumour has the typical appearance of a dysgerminoma. The prognosis is good on account of the age and sex of the patient, the type and appearance of the cells and the scarcity of mitotic figures, and because the tumour was unilateral and was removed with an intact capsule which shows no evidence of infiltration."

This type of tumour was first satisfactorily classified by Meyer² in 1931. It develops from the asexual or neuter cells of the foetal parenchyma and in the male is called a seminoma. It is often accompanied by pseudohermaphroditism or subnormal gonadal development which is not due to the influence of the tumour cells but is concomitant with the tumour. The presence of large giant cells with so-called epitheloid cells is usually characteristic and has deceived pathologists into thinking it tuberculous, and cases have been reported as "sarcoma with tuberculosis." These giant cells were not a feature in the present case. Due to the small number of reported cases

the malignancy of the tumour is not known with a great degree of accuracy but Schiller suggests it, as 10 per cent in females, 90 per cent in males (i.e. seminoma) and 50 per cent in hermaphrodites.

SUMMARY.

A case of dysgerminoma of the right ovary with acute torsion of the pedicle

occurring in a girl aged 5 years and successfully removed at operation is reported.

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ERNEST HASTINGS TWEEDY

Obituary

Ernest Hastings Tweedy

1862—1945

By the death of Ernest Hastings Tweedy of Dublin, not Eire only but Great Britain and the Dominions have lost one of the outstanding figures in obstetrics and gynaecology of the present century. It cannot be expected that a man who defeated death for 83 years can have many obstetric contemporaries left to wave him farewell, as Charon guides his faltering steps aboard, and ferries him over to the Elysian fields. Indeed, I can call to mind only Comyns Berkeley, Eden, Miles Phillips and myself. Our presence on the river's bank, could it have occurred, would certainly have heartened him greatly; and even more an assemblage of the great company of students who came under the influence of this master in obstetrics, could his passing have been staged as here suggested.

From this, the young generation, who never had the privilege of meeting him, will judge that Hastings Tweedy was a great fellow. The positions he occupied, and more especially the honours conferred on him by learned bodies, bear testimony to the high regard in which he was held by his contemporaries. The list is an impressive one—M.D. Hon. Causâ, Trinity College, Dublin; Hon. Fellow of the Royal Academy of Medicine in Ireland; Hon. Fellow of The Royal College of Obstetricians and Gynaecologists; Master of the Rotunda Hospital (1903–1910); Gynaecologist to Dr. Steevens Hospital, Dublin; President of the Obstetrical and Gynaec-

ological Section of the British Medical Association (Annual Meeting in Exeter).

These and other lesser honours are but the trappings; it is the personality of the man that his old friends especially desire to recall and to honour—in the words of Robert Burns "the man's the gowd for a' that." And his personality shone out in all he said, wrote, and did. I remember being struck by it at a little luncheon party following a session of the Congress which the late Louis Cassidy, Master of the Coombe, had organized in 1926 to celebrate the centenary of another of Dublin's great maternity hospitals. After lunch we split up into little groups. First one and then another moved over to the group at which Tweedy was holding forth as was his wont. Very soon all were around him entertained by his sallies and reminiscences, thrown off with the same informality of language and expression as when I first met him in 1892.

He joined up at the Rotunda the day before I did—so we began the serious study of obstetrics and gynaecology together. In my mind's eye I can see him as when we first met—his stocky figure in front of the mess room fire declaiming on something or someone with that exaggeration of phraseology typical of Irish humour which was never really understood or appreciated by his colleagues in London.

As can readily be realized these characteristics, coupled with his wide knowledge

of practical obstetrics and gynaecology, made him an outstanding clinical teacher. His ward visit was the event of the day and his remarks round the bedside were often recalled when in after years his old pupils foregathered.

Tweedy's most important literary work on Obstetrics was *Practical Obstetrics*, which appeared first in 1908. Wrench was his collaborator, as he was in the succeeding three editions. In the fifth edition Bethel Solomons took over from Wrench, while the last edition, the seventh, published in 1937, bears on the title page "*Tweedy's Practical Obstetrics*. Revised and largely rewritten by Bethel Solomons and Ninian Falkiner." So right down until just before the war his memory was kept fresh by former pupils and personal friends. The contributions he made to the medical journals of his time always aroused interest, and generally controversy—one recalls papers on eclampsia and its treatment with morphia; on accidental haemorrhage and his advocacy of the tampon; on obstetric shock; and one on resection of the Fallopian tubes in which he advocated the employment of strands of catgut introduced into the resected tube to maintain its patency.

Tweedy, like Smyly (whose pupil and assistant he was), was a great "Master"—incidentally they were first cousins. During the reigns of both, many additions were made and improvements introduced in the Rotunda which for well nigh two hundred years has stood out as an example of how an obstetrical and gynaecological hospital should be staffed—a Master and two Assistant Masters resident in the hospital ready to advise or to deal with any obstetrical complication. Little wonder that year after year the maternal and foetal

mortality and morbidity rates were outstandingly low. I received the other day a note from O'Donel Browne, Tweedy's son-in-law, in which there is this statement: "His seven years' mastership in the Rotunda yielded the lowest maternal mortality rate *to date*, despite the use of chemotherapy since 1936."

Tweedy took delight in his work both private and hospital. Naturally, therefore, he was beloved by all—patients, students and nurses. Then in 1922, when at his zenith, the tragedy occurred—he became totally blind and his professional life came abruptly to an end.

As might be expected the reaction to this disaster was characteristic of him—he simply added fortitude to his other great qualities. And in no small measure was he sustained in this fortitude by his beloved wife and devoted family, Major Ernest S. Tweedy, R.A.M.C., and Mrs. O'Donel Browne, to whom all we who knew him tender our deepest sympathy.

On the note of loyalty to his friends I close this very inadequate appreciation of a great spirit. Many years ago we foregathered in the hall of the Euston Hotel—I had arrived off the night train from Glasgow—Tweedy was on the point of leaving for Dublin by the day train *via* Holyhead. Without much persuasion he wired the Rotunda and postponed his departure until the following morning. We had a wonderful day together; but I can recall clearly only the finish of it. We had booked seats for some play and decided to dine at "Scotts." Looking at our watches half-way through dinner, we discovered that the play had long since started. Without more ado we tore up our tickets and ordered another bottle.

J.M.M.K.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

THE Quarterly Meeting of the Council was held in the College House on Saturday, January 27th, 1945, with the President, Mr. Eardly Holland, in the Chair.

The following candidates were elected to the Membership of the College :

Amelia Esther Burch.
James Paton Orr Erskine.
Eric Garland-Collins.
Andrew Bertram Hay.
Jadwiga Karnicki.
Gladys Elizabeth Keith.
Dorothea Mary Kerslake.
Dorothy Margaret Shotton.
Benjamin Gibson Gunlys Spiers.
Dorothy Joan Thompson.

BOOK REVIEW

"Textbook of Gynaecology." By WILFRED SHAW, M.A., M.D., F.R.C.S., F.R.C.O.G. 4th Edition. J. & A. Churchill. 24s.

IN spite of war-time difficulties there have been three editions of this book since its original publication in 1936, and both second and third editions have been reprinted. As it has thus become, in a relatively short time, one of the favourite standard works on the subject with the present-day undergraduate student, the question arises as to whether this popularity is deserved. On the whole, the book can be recommended with confidence. The material, which is logically and attractively presented, is detailed enough both to fulfil the requirements of the final examination, and, after qualification, to act as a guide to the management of gynaecological cases in general practice.

The chapters on anatomy and physiology are particularly good, and, as would be expected from such a master of the subject, the pathological descriptions are excellently written and well illustrated. Practising gynaecologists, however, find it difficult to believe that, if as stated, 15 per cent of women over the age of 35 have myomata, histology shows sarcoma in 1.5 per cent of the specimens examined.

The present edition includes new work on chemotherapy and endocrinology. Compared with the rest of the book, these sections are disappointing. Chemotherapy is discussed in dealing with gonococcal lesions, other types of acute salpingitis and urinary infections. Only sulphapyridine and sulphanilamide are mentioned and, in the chapter on gonorrhoea, it would appear that these drugs are made up in one gramme tablets. As chemotherapy is so effective in combating this infection, it would seem unnecessary to advise vaginal douching at least four times a day for chronic gonorrhoeal cervicitis.

Shaw rightly advocates care in selecting cases suitable for endocrine treatment, but he does not sufficiently stress the dangers of overdosage. Stilboestrol, being cheap to buy and easy to take, is much too readily prescribed by some general practitioners as a panacea for every gynaecological disturbance. They may be further encouraged when they find that the author would give up 15 mg. a day in some cases of amenorrhoea, 30 mg. a day for kraurosis vulvae, and 5 mg. a day, in addition to oestrin pessaries, for Trichomonad infections, particularly as he does not say how long treatment should be continued. No mention, however, is made of the use of oestrogens in the treatment of missed abortion. In contrast, the injection of 36 I.U. daily of serum gonadotropin that he recommends to promote ovulation would seem insufficient, and must be difficult to administer when the appendix at the end of the book shows that the hormone is prepared in ampoules of 100-1,000 I.U. per c.cm. This appendix, which lists the proprietary preparations along with names of the active principles they contain, is very helpful in clarifying the confusion of nomenclature made by the commercial firms.

Additions have been made to the chapter on diseases of the ovary, which has always been one of the best in the book. It is a pity no mention is made of the much-discussed Meig's syndrome, for it would be interesting to know the author's views on the subject.

Though this book can, with a little qualification, be recommended to undergraduates and practitioners, it is hardly comprehensive enough for candidates taking the higher examinations. They are not well catered for in English literature, and until a larger up-to-date textbook is available, a bibliography added to Shaw's present volume might be of help to them.

INDEX TO CURRENT LITERATURE

In this Index an endeavour will be made, so far as war conditions permit, to maintain an up-to-date record of all titles bearing on obstetrics and gynaecology and the infant. The classification aims at making immediately available for the reader the titles under the various subject headings. In the majority of instances the title is obtained from the original publication. Where this has been impossible, the title has been obtained from the abstracting journal shown in brackets. Reprints will be welcomed and should be sent to the Editor.

Any inquiries should be addressed to Miss D. F. Atkins, British Post-graduate Medical School, Ducane Road, London, W.12.

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ANATOMY

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NEW SERIES

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The Influence of Social and Economic Factors on Stillbirths and Neonatal Deaths

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It has long been recognized that infant mortality is greatly influenced by social and economic factors. In depressed areas where there are slums the mortality is high and in prosperous areas it is low. In the same city and in any area, the mortality is low in high income groups (Registrar-General's Social Class I and II) and high in low income groups (Registrar-General's Social Classes III, IV, V).^{1, 2} The social difference increases with the length of exposure to the unhealthy environment. Neonatal mortality in Class V is 50 per cent above that in Class I, but, in the age group 6 to 12 months, mortality in Class V is more than 4 times that in Class I.

It is known that in countries or areas where there is a high infant mortality, a high stillbirth-rate is also found. For example, in 1938 in Holland the stillbirth-rate was 25, the neonatal mortality-rate 21, and mortality in the period 1 to 12 months 15 per 1,000 live births. In England the corresponding figures were 38, 27 and 21, while in Scotland they were 42, 35 and 31. In the period 1939-41, the stillbirth-rate for Greater London was 30 per 1,000 total births and the infant mortality-rate 44, while during the same period the rates for Wales

were 46 and 66. These figures suggest that stillbirths are affected in a general way by the same factors as infant mortality. There are very few records of analyses of stillbirth-rates by social class and the only one available for this country is that of the Registrar-General for Scotland for the year 1939,³ when the stillbirth-rate for Scotland was 42.2 per 1,000 total births. On analysis the stillbirth-rates in the 5 social classes were 33.7, 37.8, 44.5, 38.0 and 42.3 respectively. The excess of the stillbirth-rate in Class V over that in Class I was 31.5 per cent, a much smaller social difference than is found with infant mortality.

On the other hand an analysis of maternal deaths by social class for the years 1930-32 in England and Wales showed that the maternal mortality-rate in Classes I and II was 4.44 per 1,000 births, an excess over the rate in Class V of 14.1 per cent. It might appear from these analyses that poor social and economic conditions, although they have an obvious and increasing effect on infant mortality after one month of age, have less effect on the neonatal mortality, still less on stillbirths and none at all on maternal mortality. The Report on a National Maternity Service by the Royal

College of Obstetricians and Gynaecologists* demonstrates clearly that, in fact, poor social conditions have a profound effect on maternal mortality. Similarly, further analysis of records of stillbirths and neonatal deaths suggests that poor social conditions have a serious effect on these death-rates also and that the relatively small difference in these rates between the different social classes is due to the interplay of factors which operate in opposite ways to affect mortality.

of pregnancy and many of this group are included in Group 1, since they were delivered in the same nursing home.

STILLBIRTH-RATES.

Table I shows that the stillbirth-rate in Group 1, 25.4, is less than in Group 2, 30.4. When these rates are further analysed, we see that in Group 1 the component of the total stillbirth-rate due to death of full-time infants is 16.9 and that due to deaths of premature infants 8.5. In Group 2 the corres-

TABLE I.

Analysis of Stillbirths and Neonatal Deaths in Three Groups of Cases in Aberdeen during the Years 1938-44.

| | Number | Percentage of total | Stillbirths | Stillbirth-rate | Neonatal deaths | Neonatal mortality-rate |
|-------------------------------|----------------|---------------------|-------------|-----------------|-----------------|-------------------------|
| Nursing Home Group: | | | | | | |
| Group 1, 1,419 cases | Full-time 1348 | 95.00 | 24 | 17.8 | 12 | 9.1 |
| | Premature 71 | 5.00 | 12 | 169.0 | 7 | 118.6 |
| | | | | 25.4 | | 13.7 |
| Booked Hospital Cases: | | | | | | |
| Group 2, 8,808 cases | Full-time 7999 | 90.82 | 132 | 16.5 | 131 | 16.7 |
| | Premature 809 | 9.18 | 136 | 168.1 | 164 | 243.7 |
| | | | | 30.4 | | 34.5 |
| Specialist Group: | | | | | | |
| Group 3, 501 cases | Full-time 481 | 96.01 | 4 | 8.3 | 3 | 6.3 |
| | Premature 20 | 3.99 | 1 | 50.0 | 1 | 52.6 |
| | | | | 10.0 | | 8.1 |

In order to compare stillbirth and neonatal mortality-rates in different social classes, the records of three groups of Aberdeen cases have been analysed: Group 1, a series of 1,419 delivered during the years 1938-44 in a nursing home where the expenses, apart from the doctor's fees were between 15 and 25 guineas, of whom some were under the care of specialists but the majority were looked after by the family doctor; Group 2, a series of 8,808 delivered in the Aberdeen Maternity Hospital as booked cases during the same 7 years at a cost per head of 2 pounds, all under the supervision of specialists; and Group 3, a series of 501 cases from private specialist practice. The last group was under the care of one specialist from the early months

pondering sub-rates are 15.0 and 15.4. This means that prematurity is a much more important factor in the causation of stillbirth in Group 2 than in Group 1. Although in both groups the stillbirth-rates in full-time and premature babies separately are practically the same, the total stillbirth-rate in Group 2 is higher than in Group 1 because the incidence of prematurity in Group 2 is almost double that in Group 1, and the stillbirth-rate in premature babies is 10 times the stillbirth-rate in full-time babies. In Group 3 the stillbirth-rate is only 10, due to the fact that not only is the incidence of prematurity less than in the other 2 groups, but the stillbirth-rate in both full-time and premature infants is much lower.

NEONATAL MORTALITY-RATES.

There is a much greater difference between Groups 1 and 2 in respect of neonatal mortality, the respective rates being 13.7 and 34.5. In contrast to stillbirths, the neonatal mortality-rates for both full-time and premature infants are much lower in Group 1 than in Group 2, being little more than half for full-time and less than half for premature infants. The much higher mortality-rate in premature infants in Group 2, combined with the greater incidence of prematurity in this group, accounts for much of the excess neonatal mortality in Group 2 over Group 1. The neonatal mortality-rate for Group 3 is 8.1 and the sub-rates for both full-time and premature infants are much lower than in either of the other groups.

Since there is no difference in the standard of obstetrical and nursing care between Groups 2 and 3, the difference in the stillbirth and neonatal mortality-rates is probably dependent on social status. If figures such as those quoted above are found generally, there is obviously room for great reduction in the stillbirth and neonatal mortality-rates in Scotland.

ETIOLOGY OF STILLBIRTHS AND NEONATAL DEATHS.

Stillbirths.

Postmortem examination may establish the immediate cause of foetal death but has only a limited value in indicating what measures are required to prevent stillbirths. For example, a postmortem examination may show that a child died of asphyxia or atelectasis. That explains how, not why the child died. The problem is all the more puzzling if the mother has been apparently well during the pregnancy and has had a normal labour.

In this series a postmortem examination was made of practically all cases in Group 2. The deaths have been classified accord-

ing to the clinical condition of the mother except for foetal deformity, haemorrhagic disease and other foetal conditions incompatible with life. Premature stillbirths have been classified according to the cause of the prematurity. Prematurity is not in itself a cause of death, but since premature infants are particularly liable to injury and asphyxia (the stillbirth-rate in premature infants is 10 times, and the neonatal mortality-rate more than 10 times that in full-time infants), most progress in lowering stillbirth and neonatal mortality-rates will come from prevention of prematurity. Table II is an analysis of 268 stillbirths occurring in Group 2. It shows that in 34.8 per cent of full-time stillbirths, the cause of death could not be explained adequately; that is to say, the child died *in utero* before the onset of labour, the foetal heart stopped during the course of a normal labour or the child was born with the heart still beating but failed to breathe. In respect of stillbirths in premature infants, the cause of the premature onset of labour was unknown in 33.8 per cent of the total.

Table III is an analysis of stillbirths in Group 1. It shows that the distribution of the causes of stillbirth is much the same as in Group 2 but, in full-time cases, there are fewer deaths from toxæmia and accidental haemorrhage and more from difficult labour. In Group 1 the proportion of elderly primiparae is higher than in Group 2, which would explain the higher proportion of stillbirths due to difficult labour and trauma. In Group 3, although the age and parity distribution is similar to that in Group 1, only 1 of the 5 stillbirths was associated with difficult labour. The number of cases in this group is small but it is interesting that Macafee⁵ in a series of 424 cases in private specialist practice had only 5 stillbirths, of which one was due to cerebral haemorrhage. From the results of these 2 series one might expect a stillbirth-

TABLE II.

Analysis of Causal Factors in 268 Stillbirths occurring in 8,808 "Booked" Cases in the Aberdeen Maternity Hospital during the Years 1938-44.

GROUP 2.

| Full-time infants | | | | | Premature infants | | | | |
|-------------------------------|--------|---------------------|--|--|------------------------------------|--------|---------------------|--|--|
| Causal factor | Number | Percentage of total | | | Cause of premature onset of labour | Number | Percentage of total | | |
| Unknown | 46 | 34.8 | | | Unknown | 46 | 33.8 | | |
| Difficult labour | 41 | 31.1 | | | Eclamptic toxæmia | 29 | 21.3 | | |
| Eclamptic toxæmia | 18 | 13.6 | | | Foetal deformity | 19 | 14.0 | | |
| Accidental haemorrhage | 10 | 7.6 | | | Accidental haemorrhage | 13 | 9.6 | | |
| (Without toxæmia) | | | | | Intercurrent disease | 9 | 6.6 | | |
| Foetal deformity | 8 | 6.1 | | | Placenta prævia | 6 | 4.4 | | |
| Miscellaneous | 9 | 6.8 | | | Miscellaneous | 14 | 10.3 | | |
| Total | 132 | 100 | | | Total | 136 | 100 | | |

TABLE III.

Analysis of Causal Factors in 36 Stillbirths occurring in 1,419 Nursing Home Cases during the Years 1938-44.

GROUP I.

| Full-time infants | | | | | Premature infants | | | | |
|-------------------------------|--------|---------------------|--|--|------------------------------------|--------|---------------------|--|--|
| Causal factor | Number | Percentage of total | | | Cause of premature onset of labour | Number | Percentage of total | | |
| Unknown | 10 | 41.7 | | | Unknown | 5 | 41.7 | | |
| Difficult labour | 11 | 45.8 | | | Eclamptic toxæmia | 4 | 33.3 | | |
| Eclamptic toxæmia | 2 | 8.3 | | | Foetal deformity | 1 | 8.3 | | |
| Accidental haemorrhage | — | — | | | Accidental haemorrhage | 2 | 16.7 | | |
| Foetal deformity | 1 | 4.2 | | | | | | | |
| Miscellaneous | — | — | | | | | | | |
| Total | 24 | 100 | | | Total | 12 | 100 | | |

rate of 10 with only 20 per cent of it due to trauma. In Group 1, the corresponding rate is 25.4 with 40 per cent of it due to trauma.

Conversely, as presumably avoidable factors such as trauma are eliminated by better obstetrical care, unavoidable causes such as foetal deformity account for a larger proportion of stillbirths. In Group 1 foetal deformity accounted for 4.2 per

cent of the total stillbirths; in Group 3, combined with Macafee's series, it accounted for 40 per cent.

In the Registrar-General's analysis of causes of stillbirth in Scotland in the year 1939,² the total stillbirth-rate was 42.3 per 1,000 total births. It was found that "ill-defined" causes, e.g., asphyxia, debility, atelectasis, macerated foetus and prematurity, accounted for 23.4 per cent

of the total and the cause of the stillbirth was unknown in 9.5 per cent. Therefore in 32.9 per cent a satisfactory cause of stillbirth was not found. These findings are in keeping with the Aberdeen figures in the 3 groups under review.

labour is evident in the history of mortality in the highest social classes. Table IV, which is an analysis of the trend of mortality in nursing home cases in Aberdeen since 1933, shows a steady fall in the stillbirth-rate, so that in 1944 it is less than a

TABLE IV.

Showing the Stillbirths and Neonatal Deaths at Different Dates in "Booked" Nursing Home Patients.

(Rates per 1,000 in brackets)

| Date:— | 1933-37 | 1938-40 | 1941 | 1942 | 1943 | 1944 |
|---------------------|-----------|-----------|----------|----------|----------|----------|
| Number of cases ... | 315 | 394 | 176 | 241 | 273 | 335 |
| Stillbirths ... | 15 (47.6) | 15 (38.1) | 5 (28.4) | 7 (29.0) | 6 (22.0) | 5 (14.9) |
| Neonatal deaths ... | 6 (20.0) | 4 (10.6) | 3 (17.5) | 3 (12.8) | 3 (11.2) | 4 (12.1) |

From the point of view of prevention of stillbirths an attempt was made in the Report on Infant Mortality in Scotland* to divide the cases in the Registrar-General's Report for 1939 into 2 groups, those arising primarily from the hazards of birth and those pre-existing in the child or mother. It was found that 38 per cent fell into the former group (hazards of birth) and 62 per cent into the latter group. When the cases in Group 2 in the present series are similarly analysed, it is found that 20 per cent of the stillbirths are in the category hazards of birth and 80 per cent in the category conditions pre-existing at birth. The total stillbirth-rate in Group 2 is 30.4 as compared to 42.3 for the whole country. Since the lower Aberdeen Maternity Hospital rate is due almost entirely to the lower proportion of stillbirths from hazards of birth, it appears as if the difference is to be attributed to better obstetrical technique during labour and not to superior health of the mothers during the antenatal period. If this is so, then there is obvious need for raising the general standard of obstetrical practice in Scotland.

The importance of careful routine antenatal care and skill in the management of

third of what it was in 1933-37. It might be argued that the improvement could be explained by advances in our knowledge of nutrition and improved diets for expectant mothers. It is true that these social classes are usually the first to take advantage of any advance in medical science. At the same time it is very doubtful if, at this economic level, there has been, so recently as 1933 or even earlier, any deficiency in nutrition sufficient to affect the stillbirth figures. It is much more likely that the improvement has been brought about mainly by better antenatal care and by improved technique during labour, with more frequent resort to specialist advice in abnormal cases. In Group 2 there appears to be little scope for further reduction in the stillbirth-rate by improved obstetrical care during the labour. Further improvement must come from better health of the mother before and during pregnancy.

NEONATAL DEATHS.

In analysing the causes of neonatal mortality, the premature infants dying have been arranged according to the cause of the premature onset of labour, since, al-

though prematurity is not in itself the cause of death, the neonatal mortality-rate in premature infants is 10 times that in full-time. The most likely way to lower the neonatal mortality-rate, therefore, is to lessen the incidence of prematurity. This is further emphasized by the fact that in 75 per cent of these premature infants the immediate cause of death was weakness and atelectasis, and death occurred within a day or two of birth, so that there was

little chance of preventing death even with the best medical and nursing care.

Table V is an analysis of 295 neonatal deaths in Group 2 and Table VI of 19 neonatal deaths in Group 1. In Group 2 30 per cent of deaths in full-time infants was due to infection, while in Group 1 there was no death from infection. Most of the deaths from infection in Group 2 occurred after the infants left hospital, an indication of the conditions under which they live. The

TABLE V
Analysis of Causal Factors in 295 Neonatal Deaths occurring in Hospital Cases.

GROUP 2.

| Full-time infants | | | Premature infants | | |
|-------------------------|--------|---------------------|------------------------------------|--------|---------------------|
| Cause of death | Number | Percentage of total | Cause of premature onset of labour | Number | Percentage of total |
| Infection | 40 | 30.6 | Unknown | 79 | 48.2 |
| Difficult labour | 33 | 25.2 | Eclamptic toxæmia | 21 | 12.8 |
| Foetal deformity | 30 | 22.9 | Twin pregnancy | 24 | 14.6 |
| Atelectasis or asphyxia | 7 | 5.3 | Accidental haemorrhage | 7 | 4.3 |
| Haemorrhagic disease | 5 | 3.8 | Placenta prævia | 12 | 7.3 |
| Unknown | 9 | 6.9 | Foetal deformity | 6 | 3.7 |
| Miscellaneous | 7 | 5.3 | Miscellaneous | 15 | 9.1 |
| Total | 131 | 100 | Total | 164 | 100 |

TABLE VI
Analysis of Causal Factors in 19 Neonatal Deaths occurring in 1,419 Nursing Home Cases
GROUP 1

| Full-time infants | | | Premature infants | | |
|---------------------|--------|---------------------|------------------------------------|--------|---------------------|
| Causal factor | Number | Percentage of total | Cause of premature onset of labour | Number | Percentage of total |
| Infection | — | — | Unknown | — | — |
| Difficult labour | — | 33.3 | Eclamptic toxæmia | 2 | 28.6 |
| Atelectasis or asph | — | 25.0 | Twin pregnancy | 1 | 14.3 |
| Foetal deformity | — | 25.0 | Accidental haemorrhage | 1 | 14.3 |
| Melaena | — | 3 | Placenta prævia | 1 | 14.3 |
| Erythroblastosis | — | — | ere accident | 2 | 28.6 |
| | 12 | | al | 7 | 100 |

greatest difference between the 2 groups is in deaths of premature infants and the fact that, in 48 per cent of Group 2 cases, the cause of the premature onset of labour is unknown emphasizes the difficulty of preventing prematurity. In Group 1, 7 out of 12 deaths in full-time infants, 58 per cent, were due to difficult labour or asphyxia, occurred within 48 hours of birth and were related to the conduct of labour. Some of

labour. In Group 2 the problem of neonatal mortality associated with difficult labour is complicated by the high incidence of contracted pelvis in this social class and its solution depends on the prevention of contracted pelvis as well as on improved management of labour.

Table VII is an analysis by age of 339 neonatal deaths occurring in the Aberdeen Maternity Hospital during the years 1941-44.

TABLE VII.

Table showing an Analysis of 339 Neonatal Deaths in the Aberdeen Maternity Hospital during the Years 1941-44.

| Day of death | | 1 | 2 | 3 | 4-7 | 2nd week | 3rd week | 4th week | Total | Per cent | |
|-----------------------------|-----------|-----|----|----|-----|----------|----------|----------|-----------|----------|--------|
| Developmental malformations | Full-time | 4 | 3 | 2 | 3 | 2 | 3 | 0 | 17 | 22 | (8.0) |
| | Premature | 3 | 0 | 0 | 0 | 1 | 0 | 1 | 5 | | |
| Intracranial haemorrhage | Full-time | 17 | 8 | 3 | 1 | 2 | 0 | 0 | 31 | 46 | (16.7) |
| | Premature | 7 | 4 | 4 | 0 | 0 | 0 | 0 | 15 | | |
| Asphyxia | Full-time | 10 | 3 | 3 | 0 | 0 | 0 | 0 | 16 | 127 | (46.2) |
| | Premature | 79 | 13 | 6 | 10 | 3 | 0 | 0 | 111 | | |
| Infection | Full-time | 0 | 0 | 1 | 0 | 3 | 6 | 1 | 11 | 43 | (15.6) |
| | Premature | 0 | 0 | 0 | 3 | 12 | 11 | 6 | 32 | | |
| Miscellaneous | Full-time | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 8 | 18 | (6.6) |
| | Premature | 3 | 1 | 2 | 3 | 1 | 0 | 0 | 10 | | |
| Inconclusive | Full-time | 0 | 0 | 1 | 1 | 1 | 0 | 1 | 4 | 19 | (6.9) |
| | Premature | 7 | 1 | 1 | 2 | 3 | 1 | 0 | 15 | | |
| Total | Full-time | 32 | 15 | 11 | 6 | 9 | 10 | 4 | 87 | 275 | |
| | Premature | 99 | 19 | 13 | 18 | 20 | 12 | 7 | 188 | | |
| No postmortem examination | Full-time | 6 | 2 | 0 | 1 | 5 | 1 | 1 | 16 | 64 | |
| | Premature | 23 | 11 | 4 | 4 | 4 | 2 | 0 | 48 | | |
| | | 160 | 47 | 28 | 29 | 38 | 25 | 12 | Total 339 | | |

235 (69 per cent)

264 (78 per cent)

these deaths are avoidable. In Group 2 the corresponding percentage is 30, and in Group 3 not one of the 4 neonatal deaths was associated with difficult labour. Although the neonatal mortality-rate in Group 1 is very low, 13, it could be reduced still further by improved management of

44 and it shows that 235, or 69 per cent, died within 3 days of birth. Postmortem examinations of 275 were made. Of these 46.2 per cent died of asphyxia and these were, with a few exceptions, premature infants. The other common cause of death in the first 3 days was intracranial haemor-

rhage. After the 3rd day the most common cause of death was infection, with 15.6 per cent; 75 per cent of the infants dying of infection were premature and, without doubt, the prematurity predisposed to the infection, usually a pneumonia occurring in a partially expanded lung.

Any large maternity hospital dealing with great numbers of ill and premature babies requires a very large staff and well equipped nurseries to prevent the occurrence and spread of infection and to obtain the best results. In 1941 the Aberdeen Maternity Hospital enlarged its nursery

days after birth. 132 of these weighed $3\frac{1}{2}$ pounds or less. These were born so prematurely that in most cases their organs had not reached a stage of development compatible with separate existence. The major problem, therefore, remains that of the prevention of prematurity.

In countries or cities where the infant mortality has fallen rapidly in recent years, the most striking improvement has been in the 1 to 12 months age group, so that now neonatal deaths form a much larger proportion of the total infant mortality. For example, in New York the

TABLE VIII.

Cause of Neonatal Death in 234 Premature Infants in Aberdeen Maternity Hospital during the Years 1941-44.

(Booked and emergency cases.)

| Birth weight in pounds | $5\frac{1}{2}$ -5 | 5-4 $\frac{1}{2}$ | 4 $\frac{1}{2}$ -4 | 4-3 $\frac{1}{2}$ | 3 $\frac{1}{2}$ -3 | Less than 3 | Total |
|---|-------------------|-------------------|--------------------|-------------------|--------------------|-------------|-------|
| Weakness or prematurity: lived less than 2 days or were feeble from birth | 11 | 20 | 18 | 22 | 27 | 88 | 186 |
| Infection | 3 | 5 | 8 | 5 | 7 | 9 | 37 |
| Erythroblastosis, foetal deformity and others | 8 | 0 | 1 | 1 | 1 | - | 11 |
| | 22 | 25 | 27 | 28 | 35 | 97 | 234 |

for premature and ill babies and appointed a whole-time nursery staff and paediatric registrar in charge. During the 4 years since then, although the number of deliveries occurring in the hospital has increased from 1,300 to 1,600 per annum, the deaths of infants from infection have fallen as follows: 1941, 20; 1942, 10; 1943, 7; and 1944, 6. Even if all the deaths from infection were eliminated, there would still remain a large number of deaths due to other causes. Some of these can be prevented by the use of special boxes, in which conditions of temperature, humidity and oxygen pressure can be accurately controlled. Table VIII shows that of 234 premature infants dying, 186 died within a few

infant mortality-rate was 57.3 in 1930 and in 1939 37.1, and Abramson⁷ has shown that while the mortality-rate for the 1 to 12 months age group in 1930, 26.7, was almost equal to the neonatal mortality-rate, 30.6, the mortality in 1939 in the 1 to 12 months age group had fallen to half the neonatal, 12.3 and 24.8 respectively. He shows further that in premature infants, the fall in the mortality-rate from 14.0 to 11.6 is accounted for by a fall in the death-rate in the period after the first day. There has been a marked decline (63 per cent) in the 7 to 29 days period, some improvement (27 per cent) in the 2 to 7 days period, and none in the deaths occurring under 1 day.

The importance of these very early neo-

natal deaths is demonstrated by the following American figures.⁸ In 1940 in the U.S.A., there were 67,866 neonatal deaths. Of these, 54,979 occurred under one week and 32,979 under one day. These figures agree with the findings in this paper that most of the neonatal deaths occur within a short time of birth and depend on the same factors as stillbirths, namely prematurity and feebleness of the baby, which we have shown to be associated with the social status of the mother.

There is much more information available about social class differences in neonatal mortality than there is for stillbirths. In 1930-32, according to the Registrar-General's analysis for England and Wales, the infant mortality-rate per 1,000 live births, attributed to premature birth, was 10.5 in Social Class I, and 19.6 in Class V, and that attributed to congenital debility 1.4 in Social Class I and 3.8 in Social Class V. When a country like Holland, where the neonatal mortality-rate is low (22 in the period 1932-36), is compared with Scotland, where the neonatal mortality-rate is high (37 for the same period), the excess mortality in Scotland is found to be in the category of prematurity and congenital debility. The figures for the 2 countries are as follows: in Holland, prematurity and congenital debility 9, congenital malformation and birth injury 7, other causes 6; in Scotland, prematurity and congenital debility 23, congenital malformation and birth injury 6, other causes 8. The neonatal mortality-rate in Holland at that period was the same as in Social Class I in England and Wales, while in Scotland the general rate was higher than in Social Class V in England and Wales. The excess of neonatal mortality of Scotland over that of Holland is due to prematurity and congenital debility, which also account for the excess neonatal mortality in Social Class V over Social Class I in England and

Wales and are obviously associated with poor social and economic conditions, affecting adversely the physique, health and nutrition of the mother.

The neonatal mortality-rates obtained by Holland and Social Class I in England and Wales of 22 and 21.7 do not represent the lowest possible. In Group 1 of the Aberdeen series, the neonatal mortality-rate was 13.7, and in Group 3, 8.1. Macafee in his series had 4 neonatal deaths out of 426, 9.4 per 1,000, and Rietz⁹ records a neonatal mortality-rate of 11.4 in Stockholm during the years 1918-22, in a series of cases in which the income per annum exceeded £600. It would appear that, where all social factors are favourable and medical and nursing standards good, the neonatal mortality-rate should not be more than 10.

THE EFFECT OF AGE AND PARITY ON THE STILLBIRTH AND NEONATAL AND MORTALITY-RATES.

Table IX shows that the stillbirth-rate is relatively high with a first pregnancy, least in a second, and thereafter rises with each pregnancy. The rate is least in women under 25 years of age and in each parity it rises with age. Table X is a similar analysis of Group 2 in the Aberdeen series and it shows the same findings. When the age group under 25 is subdivided into those under 20 years of age and those between 20 and 25 years, the primiparae under 20 years of age show a stillbirth-rate of 17.7, compared to a rate of 21 in primiparae aged 20 to 24. The same conclusions are reached when a series of 5,820 cases delivered under the domiciliary scheme in the County of Aberdeen is studied. Here the total stillbirth-rate is lower than in Group 2, 25.2. The stillbirth-rate was 9.7 in primiparae under 20 years of age, and 28 in primiparae aged 20 to 24. These figures point to the extreme importance of youth

for safe childbirth, in fact they suggest that efficiency begins to diminish over the age of 20.

In the County of Aberdeen domiciliary series, in 327 women under 25 years, having a 3rd, 4th or 5th child, the stillbirth-rate was 6. In 364 similar cases in Group 2

women having a 3rd, 4th or 5th child, the mortality-rate in the age group 25 to 34 years is lower than in the age group 24 years and under (28.6 and 33.4 per cent respectively). This may be dependent more upon the deterioration of the environment and economic position of the mother in the

TABLE IX.

Stillbirths (Legitimate) per 1,000 Children Born, by Age of Mother and Number of Previous Children, 1938.

(Annual Report of Registrar-General for Scotland, 1939.)

| Number of previous children | All ages | Age of mother | | | | | |
|-----------------------------|----------|---------------|-------|-------|-------|-------|-------------|
| | | Under 20 | 20-24 | 25-29 | 30-34 | 35-39 | 40 and over |
| 0 | 49 | 29 | 37 | 48 | 62 | 98 | 95 |
| 1 | 30 | 32 | 21 | 29 | 35 | 46 | 38 |
| 2 | 32 | 19 | 16 | 27 | 45 | 42 | 60 |
| 3 | 41 | — | 27 | 31 | 44 | 58 | 80 |
| 4 | 43 | — | 35 | 25 | 45 | 61 | 60 |
| 5 | 43 | — | 25 | 30 | 38 | 52 | 72 |
| 6 | 53 | — | — | 35 | 38 | 66 | 78 |
| 7 | 59 | — | — | 30 | 33 | 68 | 91 |
| 8 | 58 | — | — | — | 48 | 49 | 96 |
| 9 | 61 | — | — | — | 26 | 66 | 82 |
| 10 and over | 86 | — | — | — | 30 | 106 | 90 |
| Total | 42 | 29 | 29 | 36 | 46 | 62 | 77 |

the rate was 13.7. In 1,371 women, aged 25 to 34 years in Group 2, having a 3rd, 4th or 5th child, however, the stillbirth-rate was 32.1. Despite the fact that in all probability the pregnancies would be better "spaced" in the older age group, the stillbirth-rate is more than double that in women under 25. Rapid childbearing up to a 4th or 5th does not seem to increase the risk for the child, provided the mother is young.

Table X shows an analysis of neonatal deaths similar to that of stillbirths. The neonatal mortality-rate varies with age and parity in much the same way as does the stillbirth-rate, although the variations are much less striking. The advantage of youth is much less obvious. In fact in

younger age group, resulting from rapidly repeated pregnancy, than on deterioration of reproductive efficiency.

Table XI is a similar analysis of stillbirths in Group 1 and Group 3 cases. Unfortunately the age and parity were known only for the last 846 of Group 1, so that numbers are small when the cases are subdivided but in certain subdivisions they are large enough to allow valid comparisons to be made with Group 2. For example, in the age group 25 to 34, in Group 3, there was no stillbirth in 199 cases; in Group 1 the stillbirth-rate was 11.7 and in Group 2, 53.4. The total stillbirth-rate in primiparae in Group 2 is 44 per cent in excess of that in Group 1 and 236 per cent in excess of that in Group 3, despite the fact that

TABLE X
Stillbirth-rates and Neonatal Mortality by Age and Parity of Mother
Booked Hospital Cases, Group 2
Stillbirths

| Parity | Under 25 | | 25-34 | | 35 + | | All ages | |
|--------------|-----------------------|------------------|-----------------------|------------------|-----------------------|------------------|-----------------------|------------------|
| | Number of live births | Stillbirths Rate | Number of live births | Stillbirths Rate | Number of live births | Stillbirths Rate | Number of live births | Stillbirths Rate |
| 1 | 2131 | 19 | 1237 | 66 | 168 | 11 | 3836 | 129 |
| 2 | 858 | 11 | 1135 | 23 | 152 | 9 | 2115 | 13 |
| 3, 4, 5 | 361 | 5 | 1371 | 11 | 361 | 12 | 2096 | 61 |
| 6, 7, 8 | 8 | 0 | 296 | 9 | 211 | 12 | 515 | 21 |
| 9 + | — | — | 38 | 1 | 118 | 10 | 186 | 11 |
| All parities | 3661 | 65 | 4077 | 116 | 1070 | 57 | 8808 | 268 |

Neonatal mortality

| Parity | Under 25 | | 25-34 | | 35 + | | All ages | |
|--------------|-----------------------|-------------------------|-----------------------|-------------------------|-----------------------|-------------------------|-----------------------|-------------------------|
| | Number of live births | Neonatal Mortality-rate | Number of live births | Neonatal Mortality-rate | Number of live births | Neonatal Mortality-rate | Number of live births | Neonatal Mortality-rate |
| 1 | 2382 | 78 | 1171 | 53 | 151 | 6 | 3707 | 137 |
| 2 | 817 | 25 | 1112 | 29 | 113 | 7 | 2102 | 61 |
| 3, 4, 5 | 359 | 12 | 1327 | 38 | 319 | 11 | 2035 | 61 |
| 6, 7, 8 | 8 | — | 287 | 11 | 229 | 12 | 521 | 26 |
| 9 + | — | — | 31 | 2 | 138 | 5 | 172 | 7 |
| All parities | 3596 | 115 | 3031 | 136 | 1013 | 11 | 8510 | 295 |

1st pregnancy 43.6 per cent
2nd pregnancy 24.3 " "
3rd, 4th and 5th pregnancy 23.8 " "
6th + pregnancy 8.3 " "

TABLE XI.
Analysis of Stillbirth-rates and Neonatal Mortality in Nursing Home: Group 1 and Specialist Cases: Group 3 by Age and Parity of Mother.
 Nursing Home: Group 1.
 Stillbirths

| Parity | Under 25 | | 25-34 | | 35+ | | All ages | |
|--------------|------------------|-------------|------------------|-------------|------------------|-------------|------------------|-------------|
| | Number of births | Stillbirths | Number of births | Stillbirths | Number of births | Stillbirths | Number of births | Stillbirths |
| | Rate | Rate | Rate | Rate | Rate | Rate | Rate | Rate |
| 1 | 102 | 3 | 341 | 4 | 73 | 5 | 516 | 12 |
| 2 | 17 | 1 | 166 | 2 | 65 | 1 | 248 | 4 |
| 3, 4, 5 | | | 32 | 0 | 49 | 2 | 81 | 2 |
| 6+ | | | | 0 | 1 | 0 | 1 | 0 |
| All parities | 119 | 4 | 539 | 6 | 188 | 8 | 846 | 18 |
| | | | | 11.1 | | 12.5 | | 21.3 |

Neonatal mortality

| Parity | Under 25 | | 35+ | | All ages | |
|--------------|-----------------------|-------------------------|-----------------------|-------------------------|-----------------------|-------------------------|
| | Number of live births | Neonatal Mortality-rate | Number of live births | Neonatal Mortality-rate | Number of live births | Neonatal Mortality-rate |
| | deaths | rate | deaths | rate | deaths | rate |
| 1 | 99 | 1 | 337 | 5 | 68 | 0 |
| 2 | 16 | 0 | 164 | 1 | 64 | 1 |
| 3, 4, 5+ | | | 32 | 0 | 48 | 0 |
| All parities | 115 | 8.7 | 533 | 6 | 180 | 1 |
| | | | | 11.3 | | 5.6 |

1st pregnancy ... 61.0 per cent
 2nd pregnancy ... 29.3 " "
 3rd, 4th and 5th pregnancy 9.6 " "

TABLE XI (Continued).
Specialist Cases: Group 3.
Stillbirths

| Parity | Under 25 | | 25-34 | | 35+ | | All ages | | | | | |
|--------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------------------|------|-----|------|------|
| | Number of births | Stillbirths Rate | Number of births | Stillbirths Rate | Number of births | Stillbirths Rate | Number of births | Stillbirths Rate | | | | |
| 1 | 56 | 2 | 35.7 | 0 | 0 | 45 | 1 | 22.2 | 300 | 3 | 10.0 | |
| 2 | 9 | 0 | 0 | 85 | 0 | 29 | 0 | 0 | 123 | 0 | 0 | |
| 3, 4, 5 | 1 | 0 | 0 | 48 | 1 | 29 | 1 | 34.5 | 78 | 2 | 25.6 | |
| All parities | 66 | 2 | 30.3 | 332 | 1 | 3.0 | 103 | 2 | 19.4 | 501 | 5 | 10.0 |

Neonatal mortality

| Parity | Under 25 | | 25-34 | | 35+ | | All ages | | | |
|--------------|-----------------------|--------------------------|-----------------------|--------------------------|-----------------------|--------------------------|-----------------------|--------------------------|---|-----|
| | Number of live births | Neonatal Mortality- rate | Number of live births | Neonatal Mortality- rate | Number of live births | Neonatal Mortality- rate | Number of live births | Neonatal Mortality- rate | | |
| 1 | 54 | 0 | 0 | 199 | 3 | 15.1 | 44 | 0 | 0 | |
| 2 | 9 | 0 | 0 | 85 | 0 | 0 | 29 | 0 | 0 | |
| 3, 4, 5 + | 1 | 0 | 0 | 47 | 1 | 21.3 | 28 | 0 | 0 | |
| All parities | 64 | 0 | 0 | 331 | 4 | 12.1 | 101 | 0 | 0 | |
| | | | | | | | | 496 | 4 | 8.1 |

1st pregnancy ... 59.9 per cent
2nd pregnancy ... 24.5 " "
3rd, 4th and 5th pregnancy 15.6 " "

age and parity distribution, as appears from Table IX of national figures, is greatly in favour of a stillbirth-rate lower in Group 2 than in either of the other groups. In Group 2, 63.4 per cent of the primiparae are under 25 years of age; in Group 1 only 19.8 per cent are in this age group, and in Group 3, 18.7 per cent. Since the standard of medical and nursing care is the same in Groups 2 and 3, the excess stillbirth-rate in primiparae (236 per cent) of Group 2 over Group 3 must be due to social and economic factors. The excess is minimized by the favourable age distribution in Group 2 (the percentages of all primiparae in Group 2, in the age groups, under 25, 25 to 34 and 35 and over are 63.4, 32.2 and 4.4 respectively and in Group 3, 18.7, 66.3 and 15.0 respectively). If Group 2 had the same large percentage as Group 3 of primiparae in the 25 to 34 age group, the excess of the stillbirth-rate of Group 2 over Group 3 would obviously be greatly increased since, in this age group, the stillbirth-rate in Group 2 is 5 times that in Group 1.

As regards the effect of high parity in Group 2, 8.3 per cent have had more than 5 previous pregnancies and in these the stillbirth-rate is 47.9. There is only one case in this category in Groups 1 and 3.

It has been shown in the Report on Infant Mortality in Scotland (1943) that despite unfavourable age and parity distribution, certain areas may have a low stillbirth-rate. Greater London, with a worse-than-average age and parity distribution has the lowest stillbirth-rate of all the large cities in England and Wales. In Scotland the age and parity distribution is more favourable to a low stillbirth-rate than in any of the English areas but its actual rate is higher than any except North IV and the 2 Welsh areas. The 2 worst areas in England and Wales, North IV and Wales I show an excess stillbirth-rate at all ages. In the age groups 20 to 24, the excess

over London is 50 per cent. This cannot be attributed to closeness of the spacing of births and consequent higher average parity, because the general distribution shows no definite increase, even with the 4th birth in this age group. Hence there are influences operating in Wales and the North of England which increase the still birth-rate even between the ages of 20 and 25, when the prospects are best. Since these are depressed areas, the influence most likely to be responsible are poor physique of the mother, poor diet during pregnancy and probably a poor standard of obstetric care.

To discover why the stillbirth-rate rises after the age of 20 and still more after the age of 25 in Group 2, the stillbirths and neonatal deaths in Group 2 have been analysed in detail and the results are shown in Table XII. Neonatal deaths have been included with stillbirths here as they are, apart from infection, due to the same causes. Under the heading "cause unknown" are included all cases in which the death could not be explained adequately by a complication of pregnancy or labour, or, in the case of premature infants, when the cause of prematurity was unknown. When a premature child survived more than 2 days and died of sepsis, the death is attributed to infection, even although the prematurity was obviously an important factor in predisposing to infection. In primiparae the most important class is "cause unknown," followed by trauma, toxæmia, foetal deformity and sepsis. With increasing age of primiparae, the mortality from toxæmia, "cause unknown" and trauma rises, there is no significant rise in the death-rate from infection and a slight fall in the mortality from foetal deformity. The same is true of the second pregnancy but thereafter the figures are much more variable, since in the younger age groups of the same parity as older age groups the more rapid

TABLE XII.
*Mortality Rates (Stillbirth and Neonatal Together) by Cause, Age of Mother
and Order of Birth.*

Booked Hospital Cases: Group 2.

| Age of mother | Birth I. | | | | Birth II. | | | |
|---|----------|-------|-----|----------|-----------|-------|------|----------|
| | Under 25 | 25-34 | 35+ | All ages | Under 25 | 25-34 | 35+ | All ages |
| Number of cases | 2131 | 1237 | 168 | 3836 | 858 | 1135 | 152 | 2115 |
| Cause of death: | | | | | | | | |
| Cause unknown | 1.35 | 3.03 | .47 | 2.06 | 1.63 | 1.41 | 2.63 | 1.58 |
| Toxaemia .. | 0.65 | 1.13 | 2.9 | 0.91 | 0.23 | 0.88 | 1.31 | 0.65 |
| Trauma .. | 0.98 | 1.53 | 2.9 | 1.21 | 0.31 | 0.11 | 1.9 | 0.51 |
| Foetal deformity .. | 0.90 | 0.88 | 0.6 | 0.88 | 0.23 | 0.61 | 0.65 | 0.16 |
| Infection .. | 0.70 | 0.88 | 1.1 | 0.78 | 0.31 | 0.61 | 1.9 | 0.55 |
| Haemorrhagic disease | — | — | — | 0.10 | — | — | — | 0.09 |
| Placenta praevia ... | — | — | — | 0.07 | — | — | — | 0.14 |
| Accidental haemorrhage (without toxæmia) | 0.21 | 0.72 | — | 0.36 | 0.11 | 0.17 | — | 0.11 |
| Miscellaneous ... | 0.28 | 0.97 | 0.6 | 0.52 | — | — | — | 0.65 |

| Birth III, IV and V. | | | Birth VI and over. | | |
|------------------------|----------|-----------|--------------------|-----------|--|
| Age of mother | Under 25 | 25-31 | 35+ | All ages | |
| Number of cases | 361 | 1,371 | 361 | 2,006 | |
| Cause of death | | | | | |
| Toxaemia ... | 2.20 | 2.26 | 1.91 | 2.19 | |
| | 0.27 (1) | 0.80 | 0.55 (2) | 0.67 | |
| Trauma ... | — | 0.36 (5) | 0.55 (1) | 0.31 | |
| | — | — | 1.66 | 0.67 | |
| Foetal deformity | 0.27 (1) | 0.51 | 0.28 (1) | 0.72 | |
| Infection ... | 0.82 (1) | 0.80 | 0.28 (1) | 0.21 | |
| | 0.27 (1) | 0.21 (3) | 0.28 (1) | 0.29 | |
| Haemorrhagic disease | — | 0.36 (5) | 0.28 (1) | 0.29 | |
| Placenta praevia ... | — | — | — | — | |
| Accidental haemorrhage | — | — | — | — | |
| (without toxaemia) | — | 0.29 (1) | 0.83 (3) | 0.33 | |
| Miscellaneous ... | 0.82 (1) | 0.36 (5) | 0.83 (3) | 0.52 | |
| | | | | | |
| | Under 25 | 25-31 | 35+ | All ages | |
| | 8 | 331 | 389 | 731 | |
| | | | | | |
| | — | 3.29 (11) | 2.57 (10) | 2.87 (21) | |
| | — | — | 1.03 (1) | 0.55 (1) | |
| | — | 0.60 (2) | 1.80 (7) | 1.23 (6) | |
| | — | — | 1.29 (5) | 0.68 (5) | |
| | — | 0.30 (1) | 1.03 (1) | 0.68 (5) | |
| | — | 0.90 (3) | — | 0.41 (1) | |
| | — | 1.20 (1) | 0.77 (3) | 0.96 (7) | |
| | — | 2.10 (7) | 0.51 (2) | 1.23 (6) | |
| | — | 0.30 (1) | 1.03 (1) | 0.68 (5) | |

succession of pregnancies has led to deterioration.

The figures for all ages together show that the combined stillbirth and neonatal mortality from toxæmia is highest in a 1st pregnancy but after the 2nd remains fairly steady. Mortality of "causes unknown" is relatively high in a 1st pregnancy, falls in a 2nd and rises steadily thereafter. As would be expected, that due to trauma is high in the 1st pregnancy, falls in the 2nd, 3rd, 4th and 5th, and thereafter rises. This rise in the high parity group is associated with malposition, such as breech presentation and prolapse of the umbilical cord. There is little change with increasing parity in the death-rate from deformity or infection. Haemorrhagic diseases are a very small group in a 1st pregnancy but become a more important cause of death with increasing parity. Placenta prævia as a cause of death rises steadily with increasing parity, as also does accidental haemorrhage without toxæmia.

The analysis shows that the increase in the combined stillbirth- and neonatal death-rates with the age of the mother in Group 2, especially in primiparae, is due to increased mortality from toxæmia, "cause unknown" and trauma. "Cause unknown" is the most important factor. This means in effect that with increasing age of the mother there are more premature babies and more feeble full-time babies, who die *in utero* before the onset of labour or who cannot stand the strain of even a normal labour. The increased mortality from trauma is explained by the well-known increase with age of prolonged and difficult labour. It is difficult to say whether disordered uterine action as a cause of difficult labour is more common at this economic level than higher in the social scale but the foetal mortality from this cause will almost certainly be higher because of the higher proportion of premature and

feeble babies. Prolonged labour from contracted pelvis is more common in the lower income group.

Numbers in Groups 1 and 3 are too small to permit of similar analysis but it is noteworthy that the total foetal mortality per cent in primiparae in the age group 25 to 34 in Group 1 is 2.65 per cent and in Group 2, 9.87. In Group 2 the mortality due to "cause unknown" is 3.03 in this age group, more than the total from all causes for the same age group in Group 1. The main cause of the excess mortality in Group 2 is the high proportion of premature and feeble babies. The capacity to produce strong and healthy babies appears to fall off rapidly in primiparae in Group 2 after the age of 20, and it is only because 66 per cent of the primiparae are under 25 years of age in Group 2 that the excess mortality over Group 1 is not very much greater. In Group 1 primiparae, on the other hand, the mortality remains low till after the age of 34. In a paper to follow, it will be shown that the women in Groups 1 and 3 are much taller than those in Group 2 and the babies heavier. There is less contracted pelvis and, although accurate criteria of the nutritional state are not available, general examination shows great differences between the two groups in the state of the teeth and gums, the texture of the skin and hair and general well-being. These appearances leave no doubt that the state of health and nutrition in Groups 1 and 3 is much superior to that in Group 2.

The problems involved in lowering the stillbirth- and neonatal death-rates are different for Groups 1 and 2. In Group 1 a high standard of care during labour must be ensured since most deaths are due to trauma, dependent on the fact that a high proportion of the women are elderly primiparae. The danger run by this group despite its favourable economic position is shown by the high stillbirth-rate of 33.7 for

Social Class I in Scotland in 1939.³ As a long-term policy measures should be introduced to encourage women in this social class to have their first baby at an earlier age. In Group 2 the primary need is to improve social and economic conditions and so raise the standard of nutrition and general health. This would result in less prematurity and fewer feeble babies. Contraceptive advice should be made more easily available to this group, as the stillbirth-rate is high after the fifth pregnancy, and few of these women wish to have more than 5 children. Since, in Scotland, about 90 per cent of the mothers are in lower income groups corresponding to Group 2 in this series, the biggest reduction in Scotland's stillbirth- and neonatal mortality-rates will result from improvement in social and economic conditions.

SUMMARY.

1. In order to compare stillbirth- and neonatal mortality-rates in different social classes, the records of 3 groups of Aberdeen cases have been analysed: Group 1, a series of 1,419 delivered in a nursing home, belonging to the Registrar-General's social classes I and II and mostly under the care of the family doctor; Group 2, a series of 8,808 booked hospital cases, under the care of specialists, belonging to social classes III, IV and V; Group 3, 501 cases in private specialist practice. In the 3 groups the stillbirth-rates were 25.3, 30.4 and 10.0 respectively, and the neonatal mortality 13.0, 34.5 and 8.1.

2. In Groups 1 and 2 the stillbirth-rates in full-time and premature infants were the same, and in each group the stillbirth-rate in premature infants was 10 times that in full-time infants. The excess mortality of Group 2 over Group 1 was due to the incidence of prematurity in Group 2 being almost double that in Group 1.

3. The patients in Groups 1 and 3 are in the same social class, and the differences in the stillbirth- and neonatal mortality-rates are probably due to different standards of obstetric care. In Group 1 the stillbirth-rate has fallen from 47.6 in the years 1933-37, to 14.9 in the year 1944. This fall is due mainly to improved obstetrics.

4. In Group 2 the stillbirth-rate is 3 times that in Group 3, although the standard of obstetrics is the same. There is very little scope for reduction in the stillbirth-rate in Group 2, except by measures designed to improve the health and nutrition of the mother.

5. The problem of the high neonatal mortality in Group 2 is largely one of the prevention of prematurity. Seventy per cent of the deaths in premature infants occurred within 48 hours of birth, most of them being too feeble to maintain a separate existence.

6. The stillbirth-rate is relatively high with first pregnancies, least in the 2nd and thereafter rises with each pregnancy. The rate rises with age in each parity. In Group 2 the stillbirth-rate in the age group 25 to 34 in primiparae is nearly 5 times that in the same age group of primiparae in Group 1.

7. The reproductive efficiency in Group 2 as measured by the stillbirth-rate falls off steadily after the age of 20, whereas in Groups 1 and 3 the fall in efficiency is delayed till the age of 30.

8. In Group 2, 63 per cent of the primiparae are under 25 years of age and in Groups 1 and 3, 19 per cent. The stillbirth-rate in the latter groups would be very high if the reproductive efficiency in these groups fell off as quickly with age as it does in Group 2.

9. Over 30 per cent of the stillbirths in full-time infants in Group 2 are due to intra-uterine death of the foetus from unex-

plained causes. The cause of the onset of premature labour is unexplained in about 50 per cent of cases in Group 2. The most probable explanation in both cases is poor health and nutrition of the mother.

10. From a national point of view, the stillbirth- and neonatal mortality-rates will be most substantially improved by improvement in the standard of health and nutrition of the mothers in Social Classes III, IV and V, corresponding to Group 2 in this series, as they constitute the vast majority.

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A Case of Arrhenoblastoma Complicating Pregnancy

BY

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THE case here described appears to be unique, for although some 60 cases of this type of tumour have been recorded, not one has occurred associated with pregnancy.

Mrs. F., 26 years of age, was a woman whose previous medical history was without particular interest. Six months before she became pregnant her appendix was removed, but no comment was made as to the condition of the pelvic organs. Three months later she suffered from vomiting for several days for which a cause was not found. She menstruated quite normally on December 14th, 1942, and the pregnancy began during the next menstrual cycle. In the following February it was found that she had glycosuria, and without complete investigation her carbohydrate intake was very severely reduced. In April she noticed that hair was growing on her abdomen, and from there spread to her chest and face, and also became luxuriant on her arms and legs. Her skin became coarse, acne developed on her face and shoulders, and this was followed by crops of boils over the area affected by the acne. About the time that she noticed hair on her face her friends began to remark on her voice, which had become deeper than before. It was impossible to discover any psychological alteration. She could offer no opinion on her sexual feelings or reflexes; her reply to a direct question was that her husband had been away from home in the forces for the past few months. She

thought she had lost weight but could produce no evidence for the opinion.

She came to the out-patient department of the Saint Mary's Hospitals, Manchester, at the end of July. She then had a masculine distribution of hair, a masculine voice and figure, except that the abdomen was distended by a 7 months' pregnant uterus, and the breasts were enlarged and showed all the usual signs of pregnancy. The foetus presented by the breech, and X-ray examination showed that the legs were extended.

The clitoris was much enlarged, but there was no alteration in the labia majora or minora. Vaginal examination showed the presence of a tumour with smooth surface, separate from the uterus, about the size of a Jaffa orange, situated in the pelvis and pushing the cervix forwards into close relation with the pubes and preventing descent of the foetal breech.

She was admitted to hospital a few days later, and remained there for 2 months. She did not show any desire to return home before delivery, probably on account of her somewhat repulsive appearance.

Although the glycosuria remained constant until 3 weeks after delivery, estimation of her blood sugar on many occasions showed that it was within normal limits. On her arrival at hospital after 5 months of severe reduction of carbohydrate intake, in addition to sugar, acetone and diacetic acid were present in her urine. but estimation of her blood sugar showed that it was

94 mg. per cent. When her diet became normal the percentage rose to 125. It is clear that she was not a true diabetic; nor was she a typical example of the glycosuria of pregnancy, for in the latter the sugar comes and goes in the urine like a will o' the wisp: it is there one day and gone the next without reason. This would appear to be an example of the "Achard-Tiers syndrome," sometimes referred to as "diabetes of bearded women." I know of no satisfactory explanation of the phenomenon.

At this time she was very anaemic, her red blood corpuscle count being 3,790,000, and the haemoglobin 55 per cent of normal. The gloom of Manchester could not be offered as a partial explanation of this anaemia for she lived some 20 miles distant, in Cheshire. X-ray of the skull showed an unusually large dorsum sellae. The Aschheim-Zondek test was positive.

Owing to the extreme efficiency of the nursing staff the lower abdomen was shaved within a few hours of admission, and the photographs were taken a fortnight later. Although they fail to show the original luxuriant growth of hair on the abdomen, they do show how rapidly it could grow again (Figs. 1, 2, 3, 4).

Her waters broke prematurely at the 37th week. There were no symptoms or signs of labour starting, but it was decided that Caesarean section should be performed at once. Moderate pressure had failed to dislodge the obstructing tumour from the pelvis, and greater force was not considered justifiable. The operation was through the upper uterine segment under local anaesthesia following morphia and scopolamine premedication. The tumour proved to be a new growth of the right ovary and was removed. The left ovary was normal with the usual rusty appearance of its surface.

Lactation began on the 4th day after delivery and was established satisfactorily. Involution of the uterus and the lochial dis-

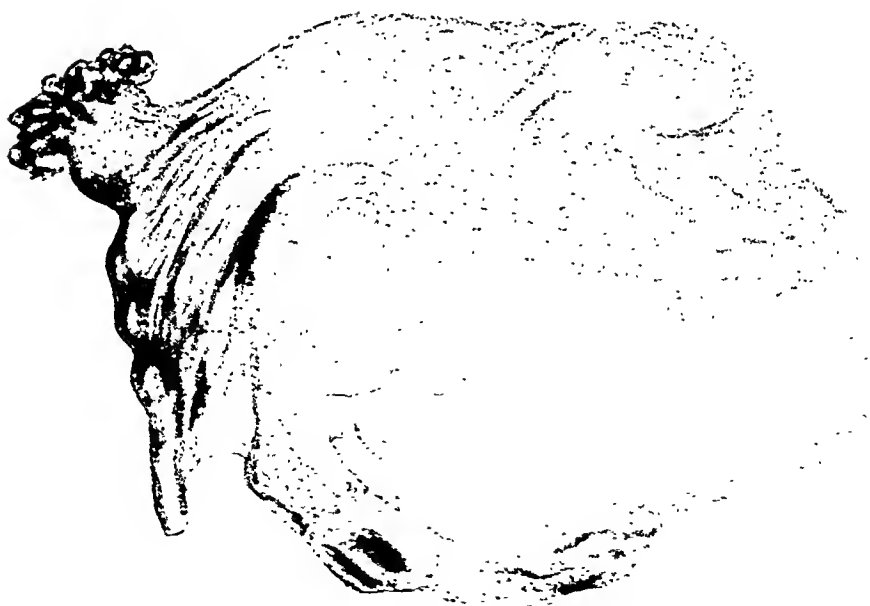
charge were about normal for a Caesarean section case.

The patient was seen 3 months after delivery, and it was found that although there was no change in her voice, yet the masculine distribution of hair was gone except for a suggestion of a moustache. The septic skin condition had continued, and her face and chest were badly scarred. There was further improvement again 3 months later; the child was still breast-fed.

There is no doubt that this is a typical case of arrhenoblastoma with characteristic symptoms and signs except where these were interfered with by the pregnancy. The reason for the extreme rarity of the combination of the two conditions is that once the tumour has produced its first symptoms, amenorrhoea, the woman is sterile, but usually several months must pass before the symptoms of virilism appear. There is, therefore, only a very short period during which pregnancy and virilism can synchronize.

Novak stresses the fact that the first symptoms of the tumour are defeminizing, amenorrhoea and atrophy of the breasts. This case showed neither of these symptoms. The amenorrhoea in her case was of pregnancy, and there was no atrophy of the breasts. It is agreed that the defeminizing phenomena are caused by the failure of the ovaries to secrete oestrin. This cessation of ovarian function is in its turn ascribed to the male hormone causing the pituitary to fail to secrete its gonadotrophic hormone. The increased secretion of both ovarian hormones from some source other than the ovary, which occurs in normal pregnancy, must have occurred in this pregnancy also, and been the cause of the enlargement and later the glandular activity of the breasts.

These new growths are described as of slow growth. Without doubt the increased vascularity of the pelvis during pregnancy



C. P. B.



Ed. Davis

PLATE I.

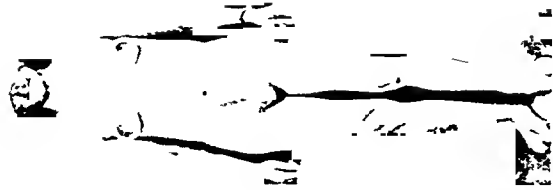


Fig. 1

Mrs. P., 34th week
of pregnancy, show-
ing masculinization
of figure
(P. II)



Fig. 2.

Showing growth of hair on face,



FIG. 3.

Showing normal pregnancy changes in breasts and the growth of hair on upper abdomen and chest; also areola on chest.

C. P. B.



FIG. 4

Showing the enlarged clitoris and the fortnight's growth of hair on the abdomen

C. P. H.

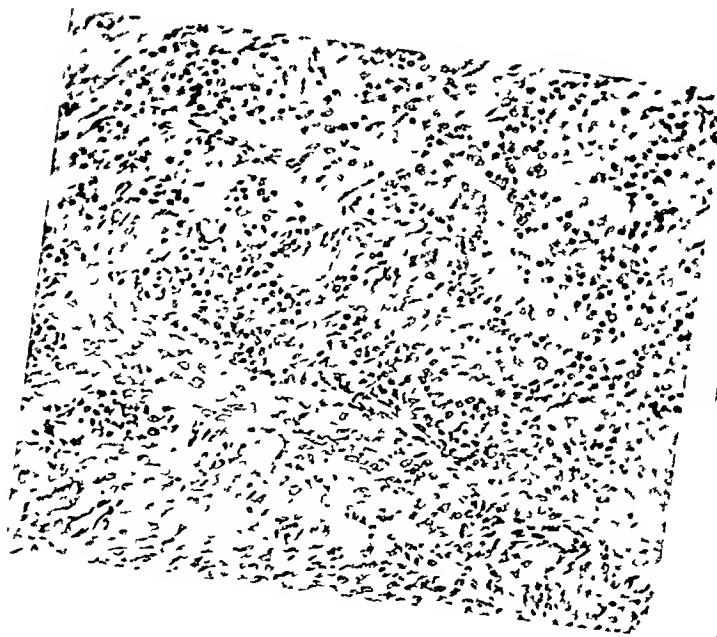


FIG 5
 Section of tumour showing on the left one of the
 fibrous bands with which the growth is intersected
 and, on the right, a cellular area
 C. P. R. x 112

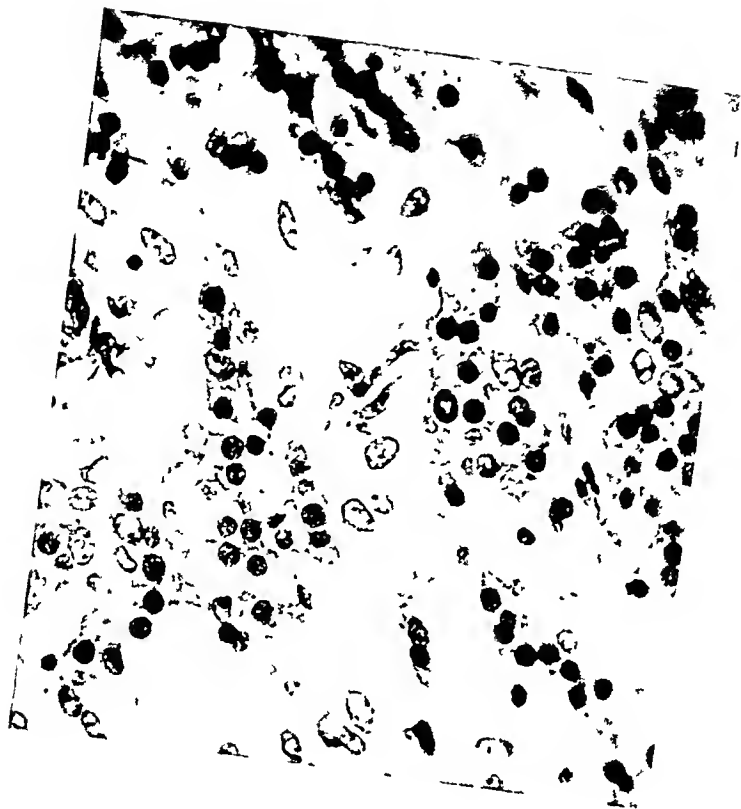


FIG 6
 High power view of one of the cellular areas, showing collections of
 cells resembling Leydig cells in a fibrous matrix
x 370



FIG. 7
Female child of Mrs. F



FIG. 8.

Child, showing enlarged clitoris, no labia minora, urethra seen with difficulty at the base of the clitoris.



FIG. 9.
Child, showing enlarged clitoris, labia majora,
enlarged and corrugated; no labia minora. Urethral
opening cannot be seen.
C.P.B.

would accelerate the rate of growth of this tumour. Judging from its size when removed in August it is justifiable to assume that it had been present for at least 12 months. From the fact that sufficient male hormone was secreted in the spring to produce masculine changes in the mother in April, it may also be assumed that a lesser quantity was being secreted at the end of the previous year, but not sufficient to interfere with the function of the pituitary gland. The quantity of the male hormone increased during the months of January and February, until in March sufficient was produced to cause the appearance of virilism in the mother in April. Usually these latter phenomena are delayed for a much longer period than this.

The tumour was of a dirty greenish colour, with a smooth tough outer coat, and in size was $3\frac{1}{2}$ by 3 by 2 inches (Plate A). It was irregularly lobulated, and its consistency varied, about one third being very hard and the remainder soft. When the growth was bisected it was clear that the hard area was a fibroma; the remainder was soft and in places cystic, somewhat resembling a degenerated fibroid, but having a pale greenish colour.

Professor J. H. Dible who examined sections of the tumour reports: "I have examined a whole section of this growth having an area of about 30 sq. cm. The tumour shows bands of well developed cellular fibrous tissue, showing well staining collagen fibres, which surround other areas made up of polygonal cells having rather an epithelial appearance scattered diffusely in a fibrous matrix. Where the latter is most developed the cells are compressed, but where it is more open or oedematous these show as groups of polyhedral cells which have abundant granular eosinophilic cytoplasm and a relatively small dark-staining nucleus: these cells resemble the interstitial (Leydig)

cells of the testicle. Fig. 5 shows these two separate appearances of the growth and Fig. 6 shows typical islets of Leydig cells.

Ovarian tumours associated with virilism are not of a single histological type and the term arrhenoblastoma has been criticized by a number of writers since it is used to suggest a functional activity of the growth and does not describe its morphology or histogenesis. For these reasons Burrows¹ prefers the word "arrhenoma," which is not open to this objection. The majority of such tumours of the ovary fall into one or other of the following histological groups.

- (a) Growths showing structures frankly resembling testicular tubules (Pick's *adenoma tubulare testiculare ovarii*).
- (b) Those showing epithelial cords without lumina, which are believed to represent the solid cords of the developing *rete testis*.
- (c) Those consisting largely of cellular fibromatous tissue which is sometimes so cellular as to be described as sarcomatous.
- (d) Teratomatous growths which may show in certain areas the development of male gonadic tissue.

Interstitial testicular (Leydig) cells are often found in the less differentiated forms, but have not been constantly reported in the tubular type of tumour. In addition, adrenal cortical tumours in the ovary may occur and produce virilism.

The growth in the present case is in the group (c) above, the members of which do not show recognizable tubular elements, but have an abundance of Leydig cells and large areas of fibromatous stroma. Attempts to demonstrate sudanophilic or lipid material in these cells in frozen sections were not very successful: a few cells showed some fatty granules, but as the only material available at this stage had been

passed through spirit, for colour preservation, no significance can be attached to this failure."

The child, which weighed 6½ pounds, appeared normal except for the external genital organs (Figs. 7, 8, 9). It may be said at once that it is almost certainly a female pseudohermaphrodite, although thorough investigation of its genito-urinary tract must obviously be postponed for several years. The clitoris was much enlarged and the glans, prepuce and frenum were well formed. The urethra opened at the base of the clitoris and behind this the perineum extended unbroken to the anus. A median raphe separated the 2 labia majora, which were enlarged and corrugated. The labia minora were absent as such. On the 4th day of life there was a discharge of blood and mucus from the urethra such as occasionally occurs from the vagina of newborn girls of this age and is usually attributed to the sudden withdrawal of maternal oestrin from the child's endometrium stimulated by that hormone. This haemorrhage was strong presumptive evidence of the presence of a uterus and a vagina opening into the urethra; and therefore of the child being a female pseudohermaphrodite.

When the mother brought the child to hospital 3 months after delivery, she reported that the haemorrhage had recurred when the child was about 4 weeks old, and again when about 8 weeks old. I have been unable to think of any possible explanation of this strange phenomenon. There has not been any similar haemorrhage since.

One naturally asks how this variety of female pseudohermaphrodite develops. There is no doubt that normally the growth or atrophy of the sex ducts, of which both male and female are provisionally laid down in the early stage of development, and the form taken by the external genital organs, including the urogenital sinus,

depend on the recently determined sex of the gonad. Although nature has made many experiments of administering male hormones to the female human mammal, with one exception all these have been adults. Nature's only experiment on the human foetus, namely the adrenogenital syndrome beginning in early foetal life, has resulted at times in a condition similar to the one here described.

The best-known of nature's experiments on mammals results in the freemartin. Here is an extraordinary and inexplicable mixture of phenomena: gonads that approach the male form, male gonoducts, but external genitalia of the female type. In the light of laboratory experiments one would have expected all the accessory genital organs to have been definitely male. Wiesner² in propounding his monhormonic theory of development suggests that this does in fact occur at times, but, because the animal is so typically male in external appearance, it is never recognized that it is really a freemartin. The evidence is against this theory, for when the freemartin is of triplets, the other 2 being male, and the concentration of male hormone is therefore doubled, its external genitalia still retain the female form.

Much experimental work has been done to investigate the results of treating pregnant mammals with androgens, Raynaud³ on mice, Dantchakoff⁴ on guinea-pigs, and Greene⁵ on rats. Greene points out that results naturally depend on 2 factors, the quantity of male hormone administered, and the period of pregnancy during which it is given, in other words dose and time. A large dose in rats in the early days of pregnancy results in resorption of the foetus. Large doses begun later in pregnancy produce in the female young a completely developed Wolffian duct and external genitalia of the male type; but in addition there are almost normal oviducts

and uterus, the latter however opening into the urethra between the Wolffian orifices at the site of the foetal Müllerian tubercle. The only possible explanation of these observations is that each gonoduct will develop normally if stimulated sufficiently early by a suitable concentration of its own sex hormone.

When the amount of androgen administered to the mother is slightly reduced there is no change in the male development; but the Müllerian duct now ends blindly, no longer opening into the urethra. Evidently the female hormone has been able to exercise some influence on the downward growth of the genital cords, and in the beginning of the development of the vagina. This influence was strong enough to close the primitive opening of the Müllerian duct, but not strong enough to cause the vagina to reach the perineum. It is interesting to recall that in 1904 Wood Jones⁶ showed that an early change in the development of the lower genital tract in the female mammal was the closure of the opening of the Müllerian duct into the urogenital sinus, and the subsequent development of the tract below this point was entirely new. One deduction may be made from this evidence, namely, that the various tissues respond unequally to the same stimulus.

The problem with regard to the external genital organs, and urogenital sinus is quite different. Here there is a collection of organs whose primordia are neutral, which may take either male or female form depending on which sex hormone dominates them. It is frequently stated that the female external genitalia including the urogenital sinus more closely resemble the foetal form than do those of the male. This view is superficial both critically and anatomically. It is true that the lower part of the sinus and adjacent structures retain more of the embryonic form, but if one

looks and dissects more deeply it is obvious at once that the upper reaches of the sinus in the male have changed little during foetal life.

Before offering any tentative suggestions to explain the male character of certain areas of this child, one must bear in mind 3 facts:

(1) There is total ignorance as to the nature and the concentration in the foetal circulation of the primitive sex hormones.

(2) It is impossible to say definitely in this case when or in what quantity the male hormone from the ovarian tumour reached the foetus.

(3) There is the unequal reaction of the various tissues of the foetus to the same quantity of the sex hormone, even if this latter were known.

It is suggested that the androgen from the ovarian tumour did not reach the foetus in effective quantity until the 3rd month of foetal life. By this time the female hormone of the foetal gonad had already produced some reactions in the accessory sex organs, probably in the upper part of the urogenital sinus. There would be the normal lag in the development of the phallus, due either to the absence of the male hormone or the presence of the female, and the urethral groove in the clitoris would be poorly developed in comparison with the corresponding groove in a penis. This poor development explains why, although the labia minora unite to advance the urethral orifice, the urethra does not canalize the clitoris. The enlargement of the clitoris cannot be called a developmental abnormality, for the same stimulus will produce enlargement of this organ in an adult, though perhaps not to the same degree.

Someone may say that this case has been reported prematurely, and that we should have waited until our knowledge about the child was complete. My answer is that one

would have to wait 3 or 4 years before more thorough investigation was attempted, and another 10 years before we could know one important fact, whether the ovaries, if there are any, would begin to function normally.

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Changes in Numbers of Circulating Blood Platelets following Experimental Traumata

BY

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INTRODUCTION.

ALTHOUGH it has long been recognized that there is an increase in the numbers of circulating platelets in the postoperative period, very little is known at present concerning the factors which bring about this change. During the 2nd week after operation, when the platelets usually reach their maximum, it is found that thrombosis occurs more frequently than at other times (Hueck,¹ Dawbarn *et al.*,² Kristensen,³ Øwre,⁴ Willinsky,⁵ Nicolaysen,⁶ Brock,⁷ Pilcher,^{8,9} Barker *et al.*,¹⁰ Wright¹¹). It has been estimated that pulmonary embolism follows about 0.77 per cent of all major operations (Barker *et al.*¹²), while from autopsies it is known that thrombosis of some degree, clinically suspected or not, occurs in a far greater proportion of patients. Burke¹³ showed by careful dissection at postmortem examinations that thrombosis at some site was present in 24 per cent of all cases, both medical and surgical, and he quotes the following figures for similar observations abroad: Germany (Bela¹⁴) 14 per cent, Australia (Cleland¹⁵) 6.3 per cent, and Switzerland (Wantoch¹⁶) 7.7 per cent. In this country Pilcher⁹ reported 261 cases of thrombosis and pulmonary embolism diagnosed clinically during 10 years at University College Hospital, London, among which the mortality-rate was 16.8 per cent, 4.6 per cent among those dying due to fatal pulmonary embolism

following an earlier clinical diagnosis of thrombosis elsewhere.

The problem of postoperative thrombosis is, therefore, one which merits considerable study, and the present series of experiments have been devised in order to throw light upon some of the factors influencing the rise in blood platelets in the critical period. A systematic experimental study of postoperative platelet changes has consequently been undertaken by subdividing the component parts of major operations into stages in order that the effects of various constituent procedures may be studied separately.

METHODS.

Platelet and red cell counts were carried out upon blood obtained by razor cuts in the marginal ear veins of rabbits. Only freely flowing blood, dropping about once a second, was used. The blood was diluted with Rees-Ecker diluting fluid, modified by the addition of 2 per cent (instead of 0.2 per cent) formalin, in order to ensure the immediate fixation of the platelets. In order to prevent any platelets adhering to the dry stem of the pipettes, diluting fluid was first drawn up to the 0.5 mark and this was followed by the same quantity of blood. Platelet and red-cell counts were both made from the same sample, by the direct wet method using a Bürcker counting chamber.

Veterinary nembutal, 1 c.cm. (60 mg.)

per kilo body weight, injected intraperitoneally, was used as anaesthetic in every instance.

OPERATIVE PROCEDURE.

Six full-grown rabbits, fed upon fresh vegetables, oats and bran, were used for this series of experiments. The interval between each operative stage in any animal was at least 5 weeks. Observations were made upon the numbers of platelets and red cells before each operation, immediately after (within 1 hour) and on the 4th, 7th, 10th, 14th and 21st postoperative days.

The graded operations were as follows:

1. *Bleeding with minimal surgical trauma.* The marginal ear vein was cut transversely with a sharp razor, care being taken not to damage the surrounding tissues. Each animal was bled 35 to 40 c.cm. (estimated to be about 25 to 30 per cent of blood volume) in 10 to 15 minutes.

2. *Simple skin incision.* Under anaesthesia, a longitudinal incision 2 to 4 cm. long was made through the skin and superficial fascia in the left paravertebral region about $1\frac{1}{2}$ cm. from the midline. The repair sutures were catgut.

3. *Skin and muscle incision.* A similar incision was made in the right paravertebral region and was extended deeply to include the skin, fascia, fibrous muscle sheath and muscle tissue to a depth of about 3 cm. Very little bleeding occurred and the tissues were repaired in three layers. Operation time was about 15 minutes.

4. *Non-surgical destruction of muscle tissue.* 2 c.cm. of a 2.0 per cent suspension of Neosyl (aluminium silicate) in normal saline was injected into the thigh muscles upon the left side, about 2 cm. below the head of the femur.

5. *Coeliotomy with manipulation of the gut.* A midline abdominal incision, passing downwards for 3 or 4 cm. from the xiphisternum was made to expose the abdo-

minal viscera. Loops of intestine were withdrawn from the abdominal cavity on to warm cloths and for 3 minutes were gently handled in a manner similar to that used when inspecting the gut systematically for a lesion in man. Care was taken not to pull upon the mesentery. The intestinal loops were replaced and the incision repaired in layers.

6. *Coeliotomy with autolysis of muscle strip.* A midline incision about $1\frac{1}{2}$ cm. in length, was made in the middle abdomen. The linea alba was opened for about 1 cm. and from the sides of this incision strips of muscle, the whole thickness of the abdominal wall, were removed. These strips were crescentic, 1-cm. long, and about $\frac{1}{2}$ cm. wide, in their central portions. They were introduced deeply between the folds of gut, care being taken to disturb the latter as little as possible. The repair of the abdominal wall was performed as before.

7. *Non-surgical sterile irritation of the peritoneum.* A low-grade peritonitis was produced by intraperitoneal injection of 5 c.cm. of 2.0 per cent suspension of Neosyl in normal saline.

8. *Splenectomy.* The figures for this stage were obtained upon a different group of 6 rabbits as it was considered undesirable to use animals after the production of peritonitis since the surgical technique would be complicated by the presence of adhesions. An incision similar to that used in Stage 2 was made. The exposed stomach was drawn forward and the spleen removed after the successive ligation of the splenic vessels without previous clamping (see Steiner and Gunn¹⁷). Repair was carried out as before.

RESULTS.

The average red-cell and platelet counts for the initial observations and for the stated postoperative days are set out in Table I.

Fig. 1 shows the average percentage change from the initial counts at various intervals after each traumatic procedure.

The immediate effect of haemorrhage (Stage 1) was to reduce the red-cell and platelet counts proportionately. Both counts returned to within normal limits by

tion to the severity of the operation. It was hardly noticeable in Stage 2 when the skin alone was damaged (10 per cent rise) and became most marked in Stages 5 and 8 when there was both muscle damage and peritoneal irritation with tissue destruction (80 and 123 per cent). In Stages 3, 4, 6

TABLE I.

| | | | Within | | | | | | |
|------------------------------|-----|-----------|---------|--------|---------|---------|----------|----------|----------|
| Day | | | Initial | 1 hour | 4th day | 7th day | 10th day | 14th day | 21st day |
| Stage 1 | ... | R.B.C.s | 6.10 | 4.52 | 4.85 | 5.14 | 5.55 | 5.77 | 6.00 |
| Haemorrhage | ... | Platelets | 549 | 350 | 420 | 512 | 500 | 529 | 546 |
| Stage 2 | ... | R.B.C.s | 5.81 | 5.79 | 5.81 | 5.38 | 5.75 | 5.81 | 5.78 |
| Skin incision | ... | Platelets | 554 | 548 | 570 | 609 | 593 | 575 | 538 |
| Stage 3 | ... | R.B.C.s | 6.02 | 5.95 | 5.88 | 5.90 | 6.09 | 6.07 | 6.00 |
| Muscle incision | ... | Platelets | 575 | 562 | 610 | 770 | 852 | 739 | 584 |
| Stage 4 | ... | R.B.C.s | 5.91 | 5.92 | 5.95 | 5.87 | 5.80 | 5.83 | 5.79 |
| Muscle destruction | ... | Platelets | 544 | 545 | 601 | 742 | 801 | 694 | 569 |
| Stage 5 | ... | R.B.C.s | 5.97 | 5.85 | 5.84 | 5.83 | 5.93 | 5.93 | 5.97 |
| Manipulation of gut | ... | Platelets | 593 | 580 | 645 | 822 | 1027 | 779 | 600 |
| Stage 6 | ... | R.B.C.s | 5.98 | 5.94 | 5.94 | 5.97 | 5.92 | 5.92 | 5.83 |
| Autolysis of muscle strip | ... | Platelets | 514 | 508 | 598 | 714 | 830 | 654 | 526 |
| Stage 7 | ... | R.B.C.s | 5.79 | 5.94 | 5.78 | 5.77 | 5.78 | 5.80 | 5.79 |
| Sterile peritonitis | ... | Platelets | 554 | 554 | 572 | 682 | 770 | 677 | 553 |
| Stage 8 | ... | R.B.C.s | — | — | — | — | — | — | — |
| Splenectomy | ... | Platelets | 541 | 541 | 805 | 1162 | 1120 | 815 | 641 |

Average red-cell and platelet counts on the various days.

R.B.C.s in millions. Platelets in thousands.

the 14th day, the restoration of the platelets being rather more rapid than that of the red cells.

The general configurations of the curves in each of the other 7 operative procedures were similar, though the extent of the response varied. In all the stages the red-cell counts remained steady throughout. The platelets, however, in all instances showed an increase in numbers, reaching a maximum in 7 to 10 days and thereafter returning to normal by the 21st day. The extent of the rise appeared to bear a direct rela-

tion to the severity of the operation. It was hardly noticeable in Stage 2 when the skin alone was damaged (10 per cent rise) and became most marked in Stages 5 and 8 when there was both muscle damage and peritoneal irritation with tissue destruction (80 and 123 per cent). In Stages 3, 4, 6

DISCUSSION.

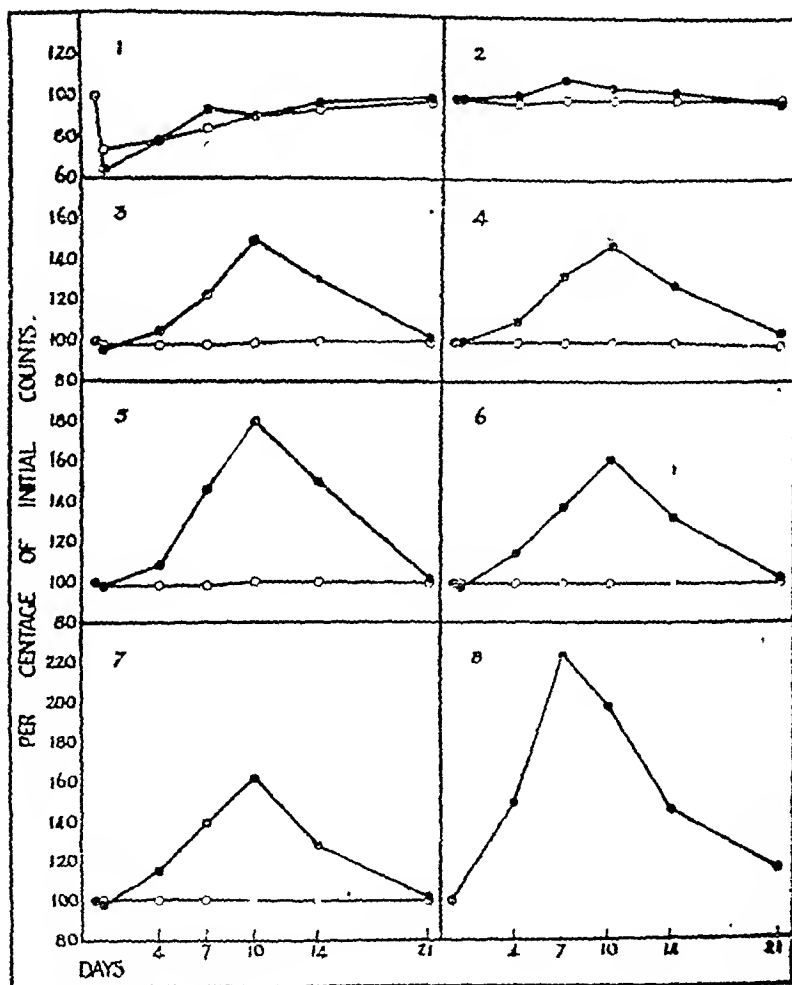
From a search of the literature upon the blood platelets changes following surgical procedures, it is surprising how piecemeal is the present state of knowledge. The wide variety of methods used for the actual

counting, together with differences of types of subjects or species of experimental animal, renders it difficult to compare the findings of the many investigations. From such observations as have been made, how-

ever, has not been elucidated. The present study, while repeating some of the observations made by previous workers has attempted to systematize the field of investigation both by using a standar

FIG. 1.

Average numbers of platelets (solid circles) and red cells (hollow circles), expressed as percentages of the initial counts on the various days following operation. Curves numbered (1-8) to correspond with the experimental stages described in the text.



ever, it is now generally believed that tissue damage is followed a week or 10 days later by a platelet response roughly proportional to the extent of the area traumatized, but the nature of the chemical stimulus con-

cerned has not been elucidated. The present study, while repeating some of the observations made by previous workers has attempted to systematize the field of investigation both by using a standar

method of platelet counting throughout and by carrying out a graded series of surgical procedures upon the same group of animals.

In 1928 Dawbarn, Earlam and Evans²

published their study upon platelet counts in man following operations and parturition. Their observations, now confirmed both clinically and experimentally by other workers, showed that haemorrhage alone was not followed by a rise in the numbers of circulating platelets, but that a rise occurred after surgical procedures. After considering several possible causes of platelet stimulation, they concluded that the only feature common to all their cases which showed the increase in platelet count, was tissue damage with the consequent absorption of autolytic products. Further, they showed that to some extent the degree of response was correlated with the extent of damage. Recently Adams¹⁸ has published a study upon a group of 51 miscellaneous surgical cases in man which showed percentage platelet elevations of a similar order to those found by Dawbarn and his associates. Adams noted that while small responses are evoked by minor operations and large ones by procedures involving much dissection and manipulation, the great majority of operations, whatever their nature, caused a remarkably constant increase in platelet numbers.

These observations, both for haemorrhage and for operations, are confirmed by the present experimental study. Haemorrhage was followed by an immediate and equal fall in both red cells and platelets. The subsequent rise in both took place steadily during the ensuing 3 weeks, but the count for the platelets never rose above that initially observed. The other procedures, viz., muscle incision, chemical destruction of muscle, autolysis of muscle strips and sterile peritonitis showed practically identical platelet responses, the increase in count being to 150 to 160 per cent of the initial figures. This percentage increase is very similar to those found in man by Dawbarn *et al.* and by Adams.

Other workers have reported elevated

platelet counts in circumstances in which there has been no surgical intervention, but in which absorption of the products of tissue autolysis has occurred. Brock and Rake¹⁹ found an increase in platelets in tubercular patients with pleural effusions, and they also showed that tuberculous rabbits when treated with tuberculin showed a similar rise. Steiner and Gunn²⁰ found a rise in platelets in rabbits following exposure to ultra-violet light and, from a comparison of these findings with those of the postoperative period, they concluded that both were due to absorption of breakdown products of injured tissues. Pohle²¹ made the same suggestion to explain the increased platelet count following menstruation in women. Fleming,²² using dogs and rats, showed that a small platelet rise of 10 to 15 per cent followed irritation of the lungs with nitrous fumes. The numbers increased in the circulation within an hour, but unfortunately observations were not made on days subsequent to the exposure. Zschau²³ showed that intravenous injection of protein solutions (casein) into rabbits was followed by a definite rise in the numbers of circulating platelets, which began about the 8th day and returned to normal in 2 to 3 weeks. Under sterile conditions he also excised strips of lumbar muscle which he then replaced in the sites of excision to undergo autolysis. The platelet increase following this procedure was very similar both in duration and extent to that following autolysis of muscle strip in the abdominal cavity in the present series. König²⁴ found that a number of proteins or protein breakdown products (casein, novoprotein, lucarnol, muscle press juice, xanthine, guanosine and adenylic acid) caused a rise in the platelet count. He concluded that it was the autolysis of nuclear material which was the chief factor in stimulating the platelet response in the postoperative period.

That the rise in platelets in the circulation is due to tissue damage is supported by the present study. The increase in their numbers following destruction of muscle with Neosyl (Stage 4) is closely comparable with that after muscle incision (Stage 3). Similarly a comparable increase occurs with sterile neosyl peritonitis (Stage 7) and with autolysis of muscle in the abdominal cavity (Stage 6). In both these latter conditions tissue breakdown products entered the blood-stream from the peritoneum. The most marked increases were observed in Stages 5 (manipulation of gut) and 8 (splenectomy) and may well have been due to the considerable tissue injury intentionally inflicted. The large rise following Stage 5 of the present series falls into line with the observations made by Dawbarn and his colleagues and by Adams, that the greater the manipulation of the gut the higher the subsequent platelet count. Splenectomy, also, is known to cause a very marked platelet response both in man (Brock and Rake¹⁹) and in animals (Liles,²¹ Steiner and Gunn,¹⁷ König,²⁴ Wright²⁶). This marked rise may be due partly to the operative trauma caused by considerable manipulation of the viscera, and partly to the extirpation of the organ which is believed to remove old or redundant platelets from the circulation.

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A Case of Retroperitoneal Haemorrhage Causing Death in Late Pregnancy*

BY

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A MARRIED woman, 30 years old, attended our antenatal clinic in the 28th week of her 2nd pregnancy. During an illegitimate pregnancy 4 years ago she had been treated for gonorrhoea and had borne normally a full-time healthy child. Evidence of venereal disease was not found now; she was very well and was sent to a clinic nearer her home for regular supervision until later pregnancy. Returning here at the 36th week for routine inspection she was found to have oedema of the legs and the blood-pressure was 160/100 mm. Hg. She was urged to stay in hospital but preferred to arrange her domestic affairs before admission. However, on the morning following her visit to the clinic she was brought in unconscious, ashen and pulseless and died within half-an-hour. At the moment of death Caesarean section was performed and a new-born, mature child was delivered. The laparotomy revealed a little dark fluid in the peritoneal cavity and a massive retroperitoneal haemorrhage on the left side. The uterus was not ruptured nor was there any evidence of other visceral injury or external violence. The bladder contained a few drops of clear urine.

The husband said that sexual intercourse had taken place during the night and twice that morning. Following this second act the wife described sharp pain in the left side, became faint and looked ghastly. He gave her tea in bed and, as she became worse, got an ambulance and brought her to hospital. She was dead in 2 hours from the beginning of the illness.

Postmortem examination (6 hours later).

The abdomen contained a great retroperitoneal blood-clot, chiefly on the left, extending from the diaphragm to the brim of the pelvis and across the midline halfway towards the ascending colon. (Fig. 1). The descending colon, pancreas and origin of mesentery of the small intestine were all pushed forward. There were, roughly, 2 litres of blood in the retroperitoneal tissues, a good proportion of it lying around the left kidney. The left broad ligament was expanded by clot to a thickness of 2 cm., but there was very little blood in the recto-vaginal septum or in the right broad ligament and none in the inferior pelvic fascia. Aneurysm or rupture was not found on dissection of the abdominal and pelvic vessels. The heart (380 g.) showed a slight left ventricular hypertrophy and scattered subendocardial haemorrhages. The aorta and its branches were elastic, smooth-

* Shown at meeting of Section of Obstetrics and Gynaecology, Royal Society of Medicine, March 16th, 1945.

walled and practically free from atheroma. The inferior vena cava was patent, but together with its tributaries had been compressed by the retroperitoneal blood-clot. The tonsils and tonsillar lymph-nodes were enlarged. There were scattered superficial erosions of the gastric mucosa. The liver (1,320 g.) was soft, friable and pale brown, its substance shrunken under a wrinkled capsule. The dorsal surface of the right lobe showed a few scattered subcapsular haemorrhages. The kidneys were normal in size and remarkably pale. Their capsules stripped easily, revealing a smooth surface. The cut surface showed a dead-white cortex of normal thickness fairly well differentiated from the medulla. The retroperitoneal blood-clot had extended along both renal arteries into the connective tissue of the pelvis. Apart from the gestational hypertrophy of the pale uterus the pelvic organs appeared normal. The spleen (110 g.) was pale and flabby. The pituitary (1.2 g.) showed gestational enlargement. The brain (1,220 g.), respiratory system, thyroid (50 g.), adrenals, pancreas and vertebral bone-marrow were all free of gross lesion.

Microscopic findings:

Liver. Numerous sections of the subcapsular haemorrhages show only dilatation and engorgement of the peripheral portion of the sinusoids of some of the lobules. In one area there is a more advanced lesion. The capillaries of the portal tract are distended and the surrounding connective tissue is infiltrated with free red cells, lymphocytes and occasional polymorphonuclears (Fig. 2). The junction of the peripheral sinusoids with the portal tracts is marked in a few places by the deposition of clumps of fibrin (Fig. 3). The cytoplasm of the neighbouring hepatic cells has been compressed, the nuclei are swollen and show an occasional mitosis (Fig. 4).

Kidney. The capillaries of the glomerular tufts show a moderate fibrillary oedematous swelling of their basement-membranes (Fig. 5). A few glomeruli show a more advanced ischaemic sclerosis and there is an early elastic hyperplasia of occasional interlobular arterioles. The afferent arterioles are normal. *Cardiac muscle.* The sub-endocardial muscle-fibres are swollen, vacuolated and degenerate and are separated by free interstitial collections of red cells (Fig. 6). *Retroperitoneal clot.* The fat is replaced by masses of red cells intersected by festoons of agglomerated platelets. The capillaries appear normal. *Stomach.* The superficial mucosal erosions are infiltrated with polymorphonuclears. Sections of the other organs do not show any striking changes except perhaps for an unusually marked development of the theca-luteal cells in the ovary.

DISCUSSION.

The pre-eclamptic clinical signs of hypertension and oedema were thus found to be based upon pathological changes in the liver, heart and kidneys typical of eclampsia.

In theory, the source of the retroperitoneal haemorrhage may have been arterial, venous or capillary. We may easily have missed a miliary congenital aneurysm (a source of spontaneous intra-abdominal haemorrhage suggested by Bruce¹), but as far as we know, such aneurysm has not as yet figured in the literature. Rupture of uterine veins in pregnancy has been described; in these cases there is gross intra-peritoneal haemorrhage.² We may have overlooked a ruptured pelvic vein in this case, but the failure of the blood to track down into the inferior pelvic fascia or into the rectovaginal septum forbids such a source. A spontaneous perirenal gross capillary oozing has been described in

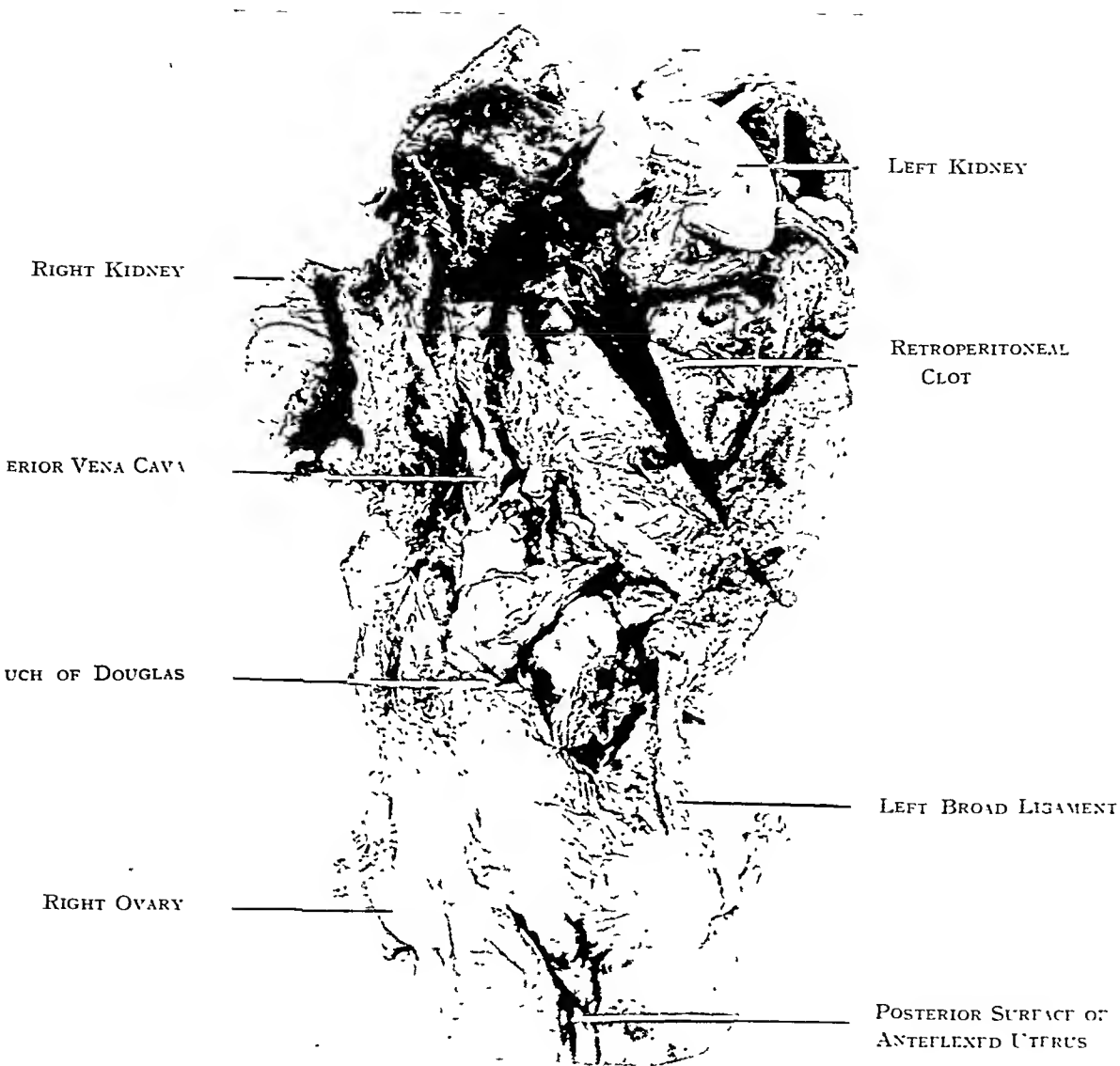


FIG. 1.

Retroperitoneal blood-clot removed at postmortem together with the kidneys, aorta, inferior vena cava and the pelvic organs. The main mass of clot can be seen around and below the left kidney.

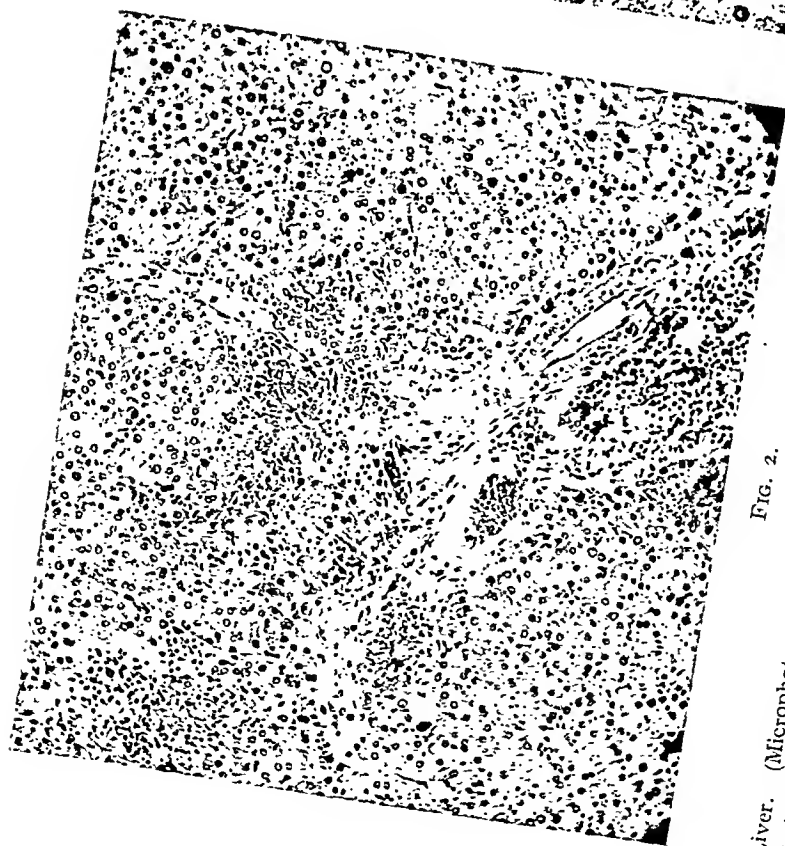


FIG. 2.

Liver. (Microphotograph $\times 112$, Formol-Zenker, Haematoxylin and Eosin.) The portal-tract-capillaries are dilated and the connective-tissue infiltrated with red cells and leucocytes.

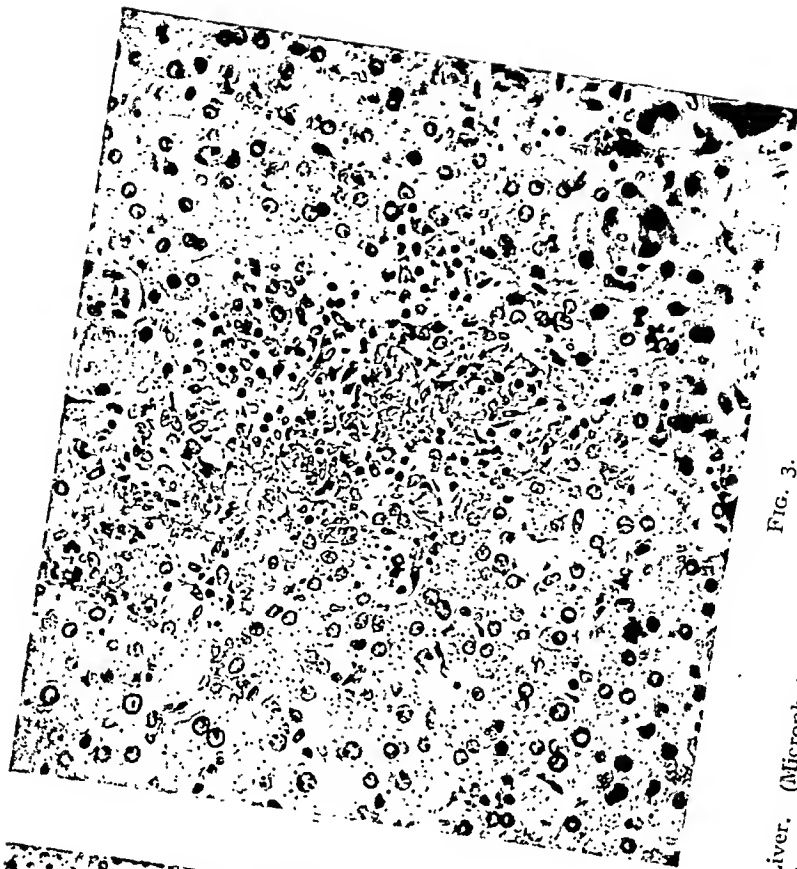


FIG. 3.

Liver. (Microphotograph $\times 240$, Formol-Zenker, Haematoxylin and Eosin.) Fibrin-deposits are seen at the centre of the field, at the junction of peripheral sinusoids with the portal-tracts.

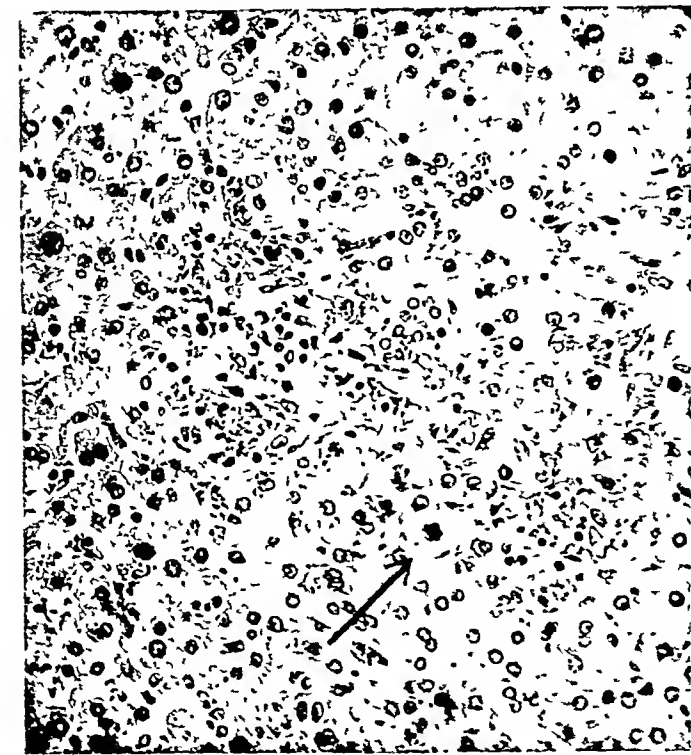


FIG 4

Liver (Microphotograph $\times 240$, Formol-Zenker, Haematoxylin and Eosin) This shows disorganisation of hepatic cells at the periphery of a lobule and a mitosis marked by an arrow



FIG 5

Kidney (Microphotograph $\times 240$, Formol-Zenker, McGregor's Azar carmine) A typical glomerulus most of whose capillaries show thicker ing of their basement-membrane A good example is marked by arrow A, contrasting with a normal capillary marked by arrow B

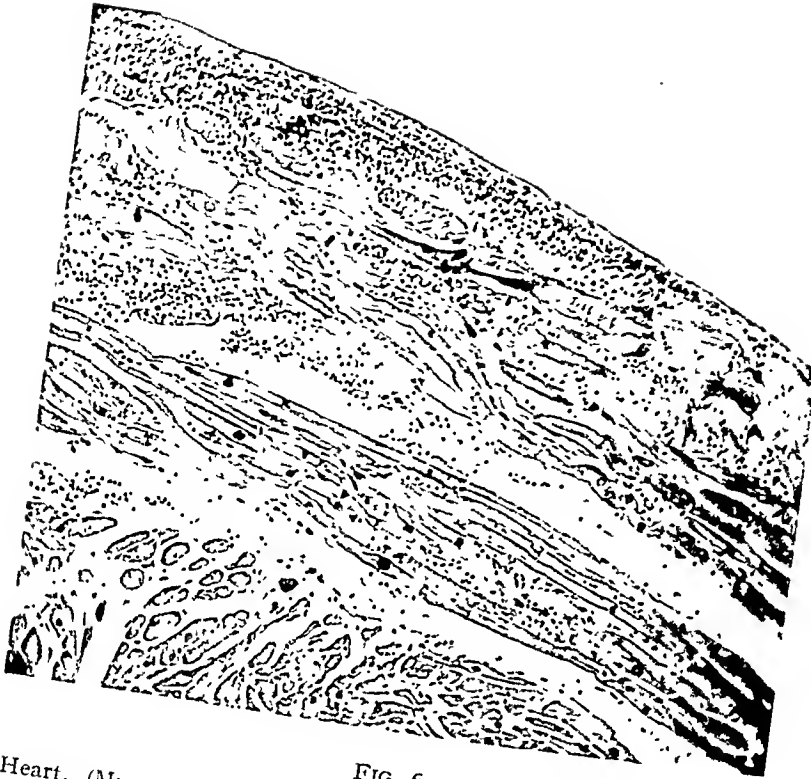


FIG. 6.
Heart. (Microphotograph $\times 122$, Formol-Zenker, Haematoxylin and
Eosin.) Swollen degenerate subendocardial muscle-fibres separated by
interstitial collections of red cells.

nephritis, leucaemia, haemophilia and hypertension by Halban and Seitz.³ Låwen,⁴ in a general article on massive retroperitoneal haemorrhage, states that it may occur in eclampsia, although he does not actually describe any cases. Our pathological findings of eclampsia on the one hand and the absence of any rupture of large vessels on the other point, therefore, to the retroperitoneal capillaries as to the source of haemorrhage. This tendency to capillary thrombosis and haemorrhage in eclampsia is, of course, well exemplified by the frequent occurrence of such lesions in the brain, liver and placental site.

It is difficult to neglect the clearcut clinical picture of trauma—the sharp onset of pain in the abdomen during coitus, the collapse, the swift demise. Trauma may well have played the part of precipitating the haemorrhage. Low⁵ has recently described a similar case of fatal retroperitoneal haemorrhage in late pregnancy which he ascribed to the strain of defaecation. Constipation was a common factor in most of the cases of spontaneous retroperitoneal haemorrhage in men and non-pregnant women reviewed by Eiss.⁶ A personal communication by an ex-colleague, Doctor Eileen Wilson, M.R.C.O.G.,⁷ tells of

“A woman aged 25, without toxæmia of pregnancy, admitted in labour to Epsom County Hospital in 1942. A full-time child was born normally after 8 hours. Twenty-six hours later, the woman collapsed suddenly with signs of internal haemorrhage and a mass was felt in the left flank from pelvis to costal margin extending across to the right flank. Blood transfusion did not effect improvement. Laparotomy was done 20 hours after

the onset of symptoms and a great clot removed from the retroperitoneal space, but further bleeding began and the woman died at once. The haemorrhage was found to have come from a ruptured aneurysm of the left renal artery.”

SUMMARY.

A case is described of massive retroperitoneal haemorrhage causing death in a woman with pre-eclamptic toxæmia in late pregnancy and following coitus. Eclamptic lesions were found in liver, kidneys and heart. The source of the haemorrhage was not discovered. The literature is reviewed

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A Series of Forty Cases of Vesicovaginal Fistula

BY

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THE problem of the vesicovaginal fistula has interested gynaecologists ever since surgery began to offer hopes of its cure. Mafouz Bey¹ has given a fine review of the history of its treatment, and Chassar Moir² has retold in detail the fascinating story of J. Marion Sims's work on this condition. At one time a terrible problem by reason of its frequency and the distress which it causes, the vesicovaginal fistula excites interest in western countries nowadays largely by its rarity and its historical associations. The difficulties of treating those cases which are encountered remain.

Where good obstetric practice is not widely available these fistulae are still fairly common. In the last 6 years I have had 40 cases admitted under my care. The series is not large compared with those that many surgeons in the East could produce—Mafouz Bey himself had treated more than 400 by 1938—but it may serve to illustrate some of the types which occur, and the results obtained, for the most part, by the flap-splitting operation. The aetiology of the obstetric fistula and the preliminary treatment have been described by many authors, and no further mention of either is therefore necessary in this paper, except to stress that this preliminary treatment is most important (anaemia and urinary sepsis are the conditions most requiring attention) and to mention that in this series one fistula was the result of a radium burn, and another the result of

lympho-granuloma, which caused the whole of the urethra to slough.

I find it convenient to classify vesicovaginal fistulae according to their situation, and under three heads. First, a fistula may lie in the vagina at an appreciable distance from the cervix and from the internal urinary meatus: a midvaginal fistula. Or it may be adjacent to the cervix, when scar tissue usually fixes it to that structure: a juxta-cervical fistula. Or it may be near to, or actually involve, the internal urinary meatus or even the urethra, a part or whole of which may have sloughed away. This it is convenient to call a juxta-urethral fistula.

In this series of 40 cases there were 18 juxta-cervical, 5 midvaginal, and 17 juxta-urethral fistulae.

All the juxta-cervical and midvaginal fistulae were operable, but 2 of the juxta-cervical cases were unfit for operation on account of their poor general condition. They went home and unfortunately did not return. The remaining 16 juxta-cervical fistulae and all of the 5 midvaginal were operated upon by the flap-splitting method. Two of each type had been operated upon before elsewhere, once or more than once. All were healed at the first attempt except 1 juxta-cervical fistula. It was not a difficult case but the patient pulled out her catheter and a pin-hole fistula remained which may have healed since, but I have been unable to trace her. The midvaginal

fistulae were most of them comparatively easy, but many of the juxta-cervical were most difficult to reach or to suture, on account of the immobility of the cervix and of bands of scar tissue which narrowed the vagina. Nevertheless, there was no case which I thought would be better approached by opening the abdomen or by opening the bladder suprapubically, and I begin to doubt whether it is often necessary to do so.

The juxta-urethral fistula were much more difficult. There were 17 cases of this type, of which 3, being unfit until the local or general condition improved, left hospital and unfortunately did not return. Of the 14 cases which remained, 2 were regarded as inoperable because in each case a large part of the inferior border of the fistula was bone: the os pubis; and it seemed, to me at least, impossible to mobilize the bladder. In the whole series there has been no other criterion of inoperability. Success was not achieved in 1 of these cases in which there was also an inoperable recto-vaginal fistula, and the other case died after transplantation of ureters from suppression of urine. Seven cases were treated by the flap method, and 5 were cured by the first attempt. One of the failures was still operable but did not return, and the other died from suppression of urine after transplantation of ureters. For each of 3 cases in which the whole of the urethra had sloughed a new urethra was made. One of these was very successful, but the other 2 became very septic and sloughed. One of them was not an obstetric fistula but the result of lympho-granuloma, and it was perhaps a mistake to attempt it, but the tissues seemed healthy and the operation carried little or no risk. The other of these failures had one ureter transplanted successfully but the patient refused to wait for the second operation, and she too must, therefore, be classed as a failure. Two cases remain to be ac-

counted for, and in each the "sacculæ" operation was performed, as described below. It failed each time, but in one of the cases both ureters were successfully transplanted, and the other case was made operable by the flap method and was thereby cured.

To sum up, 21 juxta-cervical and mid-vaginal cases submitted to operation, and 20 were cured by the flap method at the first attempt. In 14 juxta-urethral cases the patient agreed to operation. The flap method was performed for 7, with 5 successes. Three more patients were cured by other methods, making a total of 8 cures, if we may call transplantation of ureters a cure, which, strictly speaking, it is not, since the fistula remains. Combining all types: of 40 cases, 35 submitted to treatment and 28 were cured, 25 by the flap method and 3 by other means. There were 2 deaths from suppression of urine following transplantation of ureters. Two cases were regarded as inoperable, and these cases are included in the 35 which submitted to treatment. Only 4 patients submitted to a second operation: one was an unsuccessful sacculæ operation cured subsequently by the flap method, and the other 3 underwent transplantation of ureters.

I propose to describe the flap operation in some detail since this was used most frequently and with most success.

THE FLAP OPERATION.

Crossen³ classifies the various methods of operation which have been used. He recognizes two methods of flap-splitting, one from the margin of the fistula outwards towards healthy tissue, and one from healthy tissue towards the fistula. This latter method seems to be little mentioned in the literature, and little used as far as my enquiries have informed me, yet it seems to me to be immeasurably the sounder. To try to split the margins of the fistula into

vaginal and vesical flaps is to make unnecessary difficulties. It is very hard to find the plane of cleavage (the pubo-cervical fascia) by searching for it through the scar tissue of which the margin of the fistula is composed. It is, on the other hand, very easy to find it at some place remote from the fistula where there is no scarring. One makes an incision through the vaginal skin and then inserts into it a closed pair of blunt-pointed scissors, which easily finds the correct fascial layer, just as in colporrhaphy. The further procedure is described below, but it remains to consider other difficulties which dissection from the edge of the fistula brings about. First, there is the difficulty of inserting the knife into the margin of the fistula. It may be inserted into the superior margin more or less accurately and parallel with the wall of the vagina, and one may hope that it will find the pubo-cervical fascia. But it is impossible to insert the knife into the inferior margin of the fistula parallel to the vaginal wall, unless there is a marked genital prolapse and the vaginal wall can be pulled outside the ostium. One will rarely be so lucky: as a general rule the fistula is difficult to reach and genital prolapse is extremely rare, no doubt owing to the dense scarring of the vagina which is very common. But having attempted the incision there is still the difficulty of separating the vagina from the bladder. The edge of the fistula is very liable to be bruised and lacerated in the attempt, yet it is this very edge which one is to suture presently and upon which one will rely for healing. The approach described below preserves this edge from trauma and enables one to mobilize the bladder with comparative ease.

Time of operation. I prefer not less than 3 months to elapse from the last labour or last operation before a repair is attempted. If the tissues are at all oedematous they will

tear as one dissects and the sutures will not hold.

The anaesthetic. An intraspinal anaesthetic of light percaine is ideal and lasts long—a point of importance as a difficult case may take from 2 to 3 hours to complete.

The position and exposure. I have only experience of the lithotomy position. It may be necessary to pull the patient very far down, particularly when operating upon a juxta-urethral fistula. Such fistulae are often pulled upwards and around the symphysis away from the operator, and this peculiar retraction around the symphysis makes some of them very hard to reach. In such cases the patient should be pulled as far down as possible (supple Indian joints are a great help here) and then the head of the table should be lowered. It is thus possible to make the anterior vaginal wall almost perpendicular to the surgeon's line of vision and the fistula can better be seen. This manoeuvre causes the perineum to rise and obscure the view, but a para-vaginal incision will remedy this. One will often have to resort to this incision for all types of fistula; one should employ it to gain free exposure without hesitation. Bands of scar tissue in the vagina may also obscure the view, particularly in high fistulae, but one needs to think carefully where these can be divided with the greatest advantage. It is desirable to cover the repair in the bladder with vaginal skin, and it is a mistake to incise a band of scar tissue in the wrong place and to find that there is very little viable vaginal skin in the vicinity of the repair from which to fashion a flap. Generally speaking it is safe to divide scar tissue on the posterior vaginal wall, and it is usually convenient if the paravaginal incision is carried up to these bands and through them.

An Auvard's speculum is usually re-

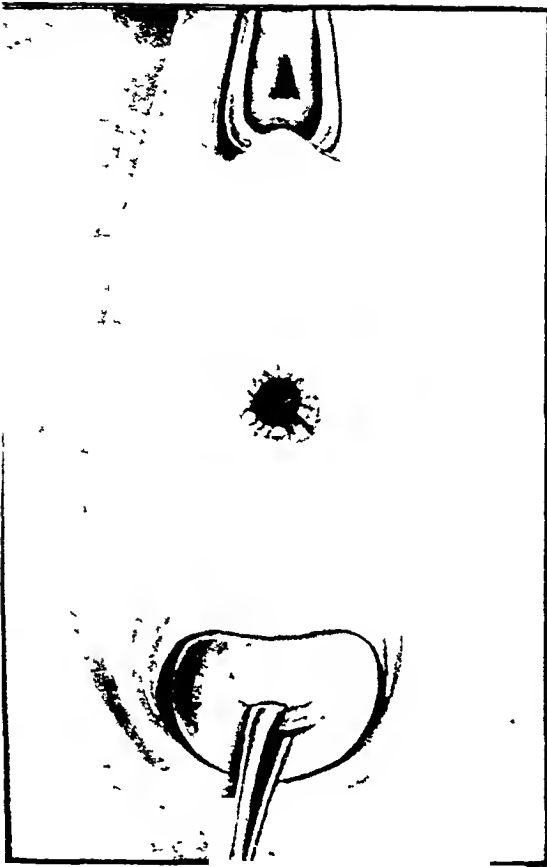


FIG 1
An easy midvaginal fistula

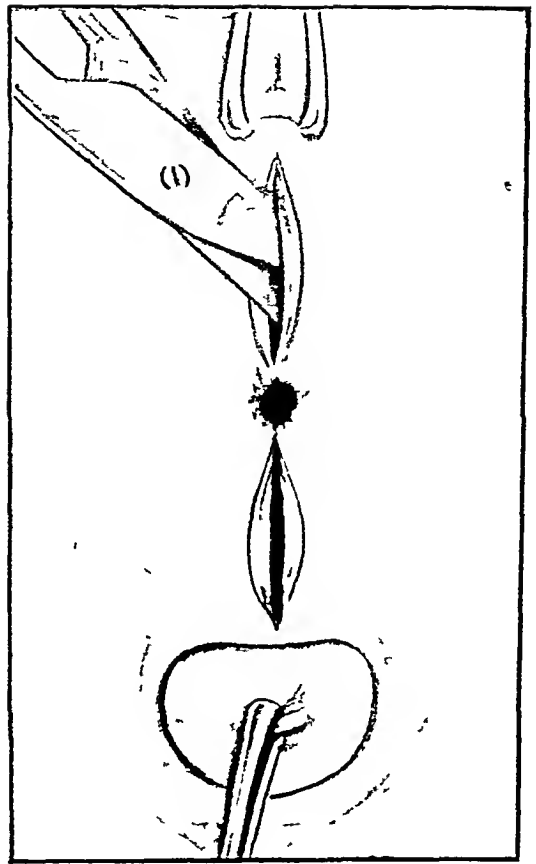


FIG 2
Both incisions have been made, and the scissors are separating the bladder from the vagina. In practice this is done first from the other (i.e. higher) incision, so that any blood which issues from it will not obscure one's work on the lower incision.

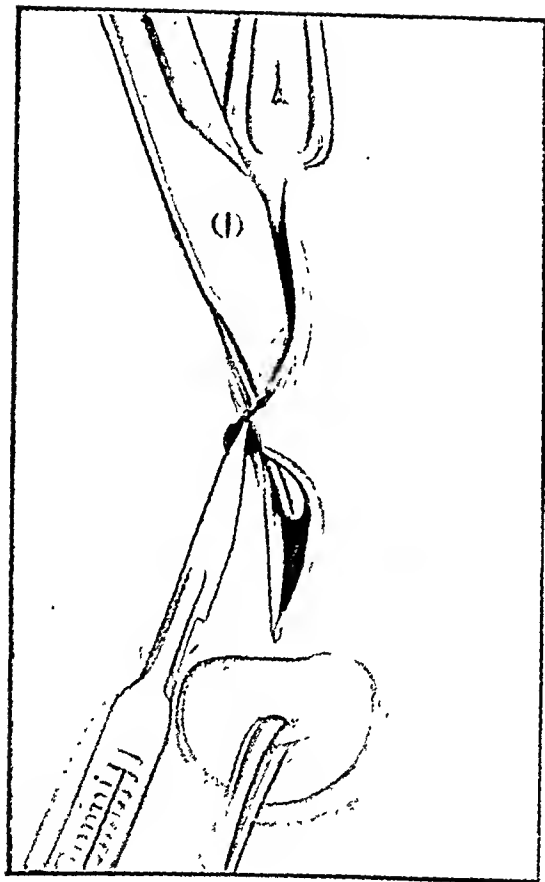


FIG. 3.

Bladder and vagina have been separated widely through each incision on each side. Only the edge of the fistula now holds them together. A No. 11 Bard-Parker knife is dividing this last connexion, cutting on to a pair of closed scissors inserted through the lower incision and emerging from the upper.



FIG. 4.

The fistula is free and the bladder has been mobilized as far as is desired. The vaginal flaps are held back by tissue forceps. Traction sutures hold the bladder steady, and the suturing of the fistula has begun. In practice the suture is held at the correct tension by an assistant, but this has not been shown.

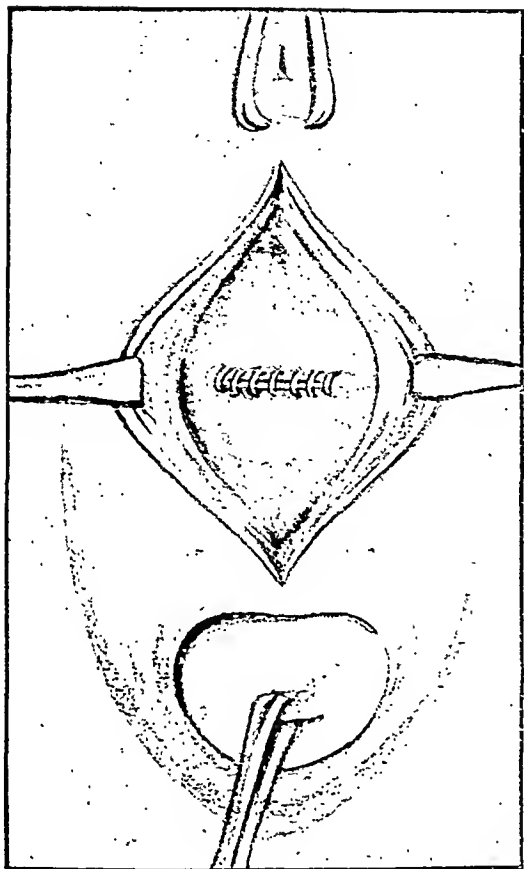


FIG. 5.

The suturing is complete and the traction sutures have been removed. It remains only to suture the anterior vaginal wall.

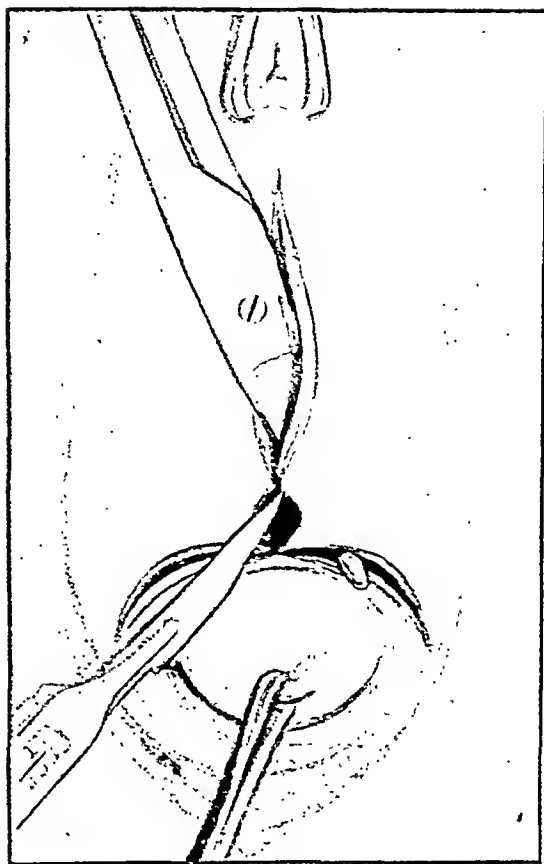


FIG. 6.

The procedure adopted for juxta-cervical fistulae. After retracting both vaginal flaps, the bladder, with the fistula, will be dissected from the front of the cervix. This dissection may also be required in the lower fistulae (midvaginal or juxta-urethral).

quired, and sometimes it is helpful to sew the labia minora to the buttocks to keep them out of the way and to open up the ostium. Finally, a volsellum is usually applied to the cervix and a tissue forceps near the lower end of the vaginal wall so that the anterior vaginal wall may be kept on the stretch while the first incision is being made. More often than not, the volsellum will have to be pushed upwards (anatomically speaking, that is) in order to stretch the vagina, since the cervix cannot be pulled down if there is no genital prolapse.

The incision. An incision is made from below upwards to the fistula through the vaginal skin, and then from the fistula upwards to the cervix (Fig. 1), except in juxta-cervical fistulae, which will be dealt with separately. The depth of the incision is the same as for colporrhaphy, and there is no particular difficulty except that usually one is working within the vagina. The points of a closed pair of Mayo's scissors, curved on the flat, are then thrust into the fascial space between the bladder and the vagina, which are then easily separated by opening the blades of the scissors (Fig. 2), again as in colporrhaphy. This manoeuvre is carried out on each side through each of the incisions, so that finally the bladder and the vagina are held together only by the adherent margins of the fistula. All around, the bladder and the vagina have been cleanly separated in a plane of cleavage easily found by this approach from a distance, where scarring is minimal or absent. With juxta-cervical fistulae the incision above the fistula towards the cervix obviously cannot be made as just described. It is made transversely across the front of the cervix, between it and the fistula, and it is then curved on each side laterally towards the fornices (Fig. 6). This may be difficult on account of scar tissue, and in one case it simplified matters to carry the paravaginal incision right up to the fistula

itself, after which separation of the lateral flap was much easier.

Freeing the fistula. A closed pair of scissors or a probe is now inserted in the inferior incision, and, if possible, made to emerge from the upper incision (Fig. 3). It is thus pressed against the scar tissue which still binds the bladder and vagina together at the margin of the fistula. A sharp knife (a No. 11 Bard Parker is very useful) is then used to cut cleanly through this margin on to the scissors or probe. This is done on each side, and thus the fistula is freed. The orifice in the bladder is clean-cut instead of lacerated, and it is fit for suturing. It has not been touched at all in the separation of the flaps.

In juxta-cervical fistulae and in the larger midvaginal ones, and even in some of the juxta-urethral, it is necessary to mobilize the bladder from the front of the cervix. This is a very common step in gynaecological operations and need not be described here. If more mobilization laterally is required, gauze dissection will supply it. The pull of the gauze is on the bladder far away from the fistula, which will not suffer any harm. It must be emphasized that adequate mobilization of the bladder, so that the fistula may be closed without any tension whatever, is absolutely essential.

Suturing the bladder. As a general rule it is easier to suture the bladder horizontally, since by this means the best advantage may be taken of the loose bladder which has been dissected from the cervix. It is useful to insert 2 traction sutures, one at each side of the orifice, not less than a $\frac{1}{4}$ inch from its edge. A gentle pull on these will prevent the loose bladder from falling away, and will keep the fistula steady and as near to the operator as possible (Fig. 4).

I have used only very fine chromicized catgut, on atraumatic needles where there was room to use them, and closed the gap with a simple continuous suture, about 12

stitches to the inch. After each stitch the catgut should be gently pulled to the right tension and kept at this tension by the assistant. If it is allowed to slacken then there is great danger of the urine leaking at this point. This may be detected before the end of the operation, but if several other sutures have been inserted each of them will have to be tightened, and in doing so one or more of them may tear out. In any case there will be the risk of fraying the edge of the fistula, which it is one's particular care to preserve from trauma. I believe it to be very important also to start and to finish the suture at least $\frac{1}{2}$ inch from the edge of the fistula, so that there may be no leakage from the ends of the suture line. The suture should pass through the bladder musculature down to, but not through, the mucosa. This, it must be admitted, is in many cases but a counsel of perfection. When the fistula is hard to reach it may be most difficult to pass a suture at all, in which case a good bite of bladder muscle probably suffices. This is certainly better than going too far and including the bladder mucosa, which invites a leak. If the mucosa prolapses through the fistula so that it is hard to avoid piercing it with the needle, then it may be trimmed with scissors. Sometimes after the suture line is completed there remains plenty of loose bladder wall, and there is little difficulty in passing a second suture line in the Lembert fashion. If, however, the bladder wall is thin, or there is not enough left to allow of easy infolding, then it is better to leave well alone. The infolding suture is certainly not essential and I have often omitted it.

Sometimes the margins of the fistula are so far out laterally that the traction sutures referred to above cannot be used, and often it is difficult even to pass a suture to close the gap. Very small needles have to be used. Frequently atraumatic sutures are

far too big, and there is too little space to manoeuvre them in. Occasionally it helps to employ 2 stitches, one passed from each side while the central portion of the hole is still open. These 2 sutures meet in the middle and are there tied together. By this means the act of suturing becomes easier as one progresses towards the middle.

It is hard to exaggerate how difficult this part of the operation may be. Several trials may be necessary, before each stitch is passed, to adjust the needle in the needle-holder so that it may be introduced up as far as the fistula and correctly inserted. The concentration necessary to do this with the least possible trauma and with great accuracy makes the operation often most fatiguing. And indeed throughout the operation each movement must be deliberate; even a little obscuring blood clot must be removed with care, for a slight tear in the bladder wall or the pulling out of a stitch may ruin the operation.

Testing the suture line. The bladder is now filled through a rubber catheter with methylene blue under a pressure of 1 or 2 feet of water. The catheter may usually be a No. 10 or 12, but a smaller one is often necessary for juxta-urethral fistulae, as a larger one may strain the suture line and cause a leak. If there is no leak, the bladder is emptied and the catheter turned to one side. Only once did I find the suture line leaking. It had been particularly difficult to sew the left extremity of the fistula which extended almost to the pubic ramus. I passed a purse-string suture around the leaking area and the repair healed, but I am bound to say that I think I was fortunate.

Suturing the vagina. Often this is fairly easy and sometimes one can usefully excise a portion of the vaginal flaps, as in colporrhaphy. In case of doubt it is better not to do so, because if the operation is a failure one will need all tissue possible for

the next attempt. There may sometimes be difficulty in making the vaginal flaps meet to cover over the repair in the bladder. Only on one occasion did I have to fashion flaps and bring them across from their original position, and the operation was a failure. On another occasion I had to leave the bladder uncovered after performing a sacculé operation, and this operation also failed, although the fistula was cured subsequently. Having sutured the vagina and also the paravaginal incision, if one has been necessary, one sutures the catheter to the labia minora. The patient does not experience any pain from this unless she tries to pull the catheter out, and she soon desists. Self-retaining catheters I have not used. They easily fall out, they are painful if their shoulders press on the trigone, and for juxta-urethral fistulae they may press on the suture line and strain it.

The vagina is now gently but firmly packed with gauze soaked in 1 in 1,000 acriflavine, which is removed after 24 hours.

After care. The main point of the after-care is to ensure that the bladder remains empty. It is therefore necessary to see that the patient does not pull out the catheter and that the catheter does not become blocked with blood clot, mucus, or phosphatic deposits. Quite a little blood may flow into the bladder through the fistula in the course of the dissection, and it is wise to clean it out before the bladder is closed. Even so, a little may be left and give trouble. For 12 days the drainage by catheter continues, and every hour, day and night, the nurse records the amount of urine which has drained. One thereby receives early warning if the catheter becomes blocked. Should it do so the bladder may fill up and strain the suture line sufficiently to make it leak. But if the block has existed for no more than one hour, then little urine will have collected

in the bladder in this short time. The catheter may be cleared by injecting up it 5 to 10 c.c. of sterile water; occasionally it may be necessary to change it. This must be done with particular care if the fistula was juxta-urethral.

My patients are nursed on their backs, but if they find this very irksome they are permitted to turn on their sides with care after 4 or 5 days. I doubt very much if nursing patients in the prone position, as some authorities recommend, can prevent the urine wetting the suture line. The anterior and posterior walls of the bladder are in contact as long as the urine is being constantly drained by catheter, and the posterior wall must, therefore, be just as wet when the patient is prone as when she is supine. Even if a suprapubic cystostomy were made the bladder walls would collapse and touch each other, and the urine is bound to wet them both. I do not think it is at all necessary to keep the suture line dry, nor do I think it possible to do so. Gastro-enterostomies heal well yet are never dry, and nobody ever attempts to keep them so, though I must admit that the comparison is not quite fair as gastro-enterostomies would probably not heal as well but for the sealing action of the peritoneum. Howbeit, it is hard to reconcile the success of the juxta-cervical fistulae in this series with the need for keeping the suture line dry. The failures in this series were, all but one, juxta-urethral fistulae, which were no wetter than the others. The failures I ascribe to difficulties in suturing and to the thinness of the urethra from which in some cases, I feel certain, the sutures cut out, despite great care to avoid tension.

Some surgeons, at the other extreme, order daily bladder wash-outs, but this practice I abandoned after my first few cases except when the catheter became continually blocked with deposits. It seems

to be unnecessary as a routine; copious drinks are effective in keeping the urine dilute, and urinary antiseptics may also be given.

The less interference the patients undergo the better, and for this reason the bowels are left alone for 10 days, before which time it is rare for them to act spontaneously. Patients do not suffer any harm or discomfort from this, and they pass a stool without difficulty when given an enema. On the 12th day the catheter is removed, and the patient is then encouraged to pass water every 2 hours for 5 or 6 days, and thereafter only when she has the inclination. It is striking how rapidly a patient begins to control her bladder, and how soon the bladder stretches to accommodate a normal amount of urine, although it has been empty and contracted for the months or years during which it has leaked from the fistula.

One final point regarding the after-treatment: one need not be unduly despondent if the patient appears to be leaking. Very often the leak is around the catheter and the repair has not broken down. One must, however, make certain that the catheter is not blocked.

After the operation patients are kept in bed for 4 weeks, and advised to avoid coitus for a further 3 months and to report early if they again become pregnant.

OTHER OPERATIONS USED.

1. *Bonney's Operation for Elongation of the Urethra.*

This operation of Bonney⁴ was adapted for 3 cases. In these there was no urethra left. It had sloughed away leaving a hole leading from the bladder directly into the vagina at the site of the internal urinary meatus. Only in 1 case was the operation successful; in the other 2 sepsis spoiled what appeared to be a sound operation.

Despite these 2 failures I feel sure that this is the ideal operation for such cases.

2. *Saccule Operation.*

This was used in 2 cases. In these the upper part of the urethra had sloughed away and there was a considerable gap between the fistula and the remains of the urethra, too big a gap to bridge by anastomosing the fistula to the top of the urethra. The aim of this operation is to turn over flaps of vaginal skin and to suture them so that they form a saccule intervening between the fistula and the urethra. The urine should flow from the fistula into the saccule and thence out through the urethra. On both occasions the saccule failed to heal, but in 1 case only a small portion remained open. This small hole (about $\frac{1}{4}$ inch in diameter) it was possible to close by the flap operation, and the patient was thereby cured.

3. *Colpocleisis.*

This unpleasant operation was attempted twice in the same patient and it failed each time. I doubt if the operation is justified unless, as in this case, there were an inoperable vesico-vaginal fistula and an inoperable recto-vaginal fistula. I thought a colpocleisis would be better than leaving the patient untreated, and she herself was of the same opinion. The tissues were like cartilage, and several attempts to cure the recto-vaginal fistula and 2 attempts thereafter to perform colpocleisis were complete failures.

4. *Transplantation of Ureters.*

This paper is not concerned with the technique of this operation, which has been well described by others. My comparatively small experience of vesicovaginal fistulae however, leads me to think that only a small percentage of them needs transplantation and that when a large series of transplants

ions is described one should enquire what percentage of the total number of fistulae seen the series represents. Too frequent performance of this operation is to be deplored. The mortality-rate is bound to be higher than in the repair operation: Murray and Ahmed⁵ report a mortality-rate of 21.5 per cent. The result is nothing like so satisfactory as a repair, and further it is not a cure of the fistula, although it certainly gives relief.

HEALED FISTULA AND SUBSEQUENT DELIVERIES.

Not all fistulae, by any means, are due to disproportion. Nevertheless, I feel that all subsequent deliveries, if circumstances permit, should be by classical Caesarean section. In a vaginal delivery the descent of the head is bound to stretch the scar of a healed fistula, and the risk of its tearing must be considerable. Caesarean section does not seem too big a price to pay as an insurance against so unfortunate an occurrence. Even Case No. 23, in which a natural delivery took place within 2 hours of labour starting without any difficulty at all, does not alter this opinion. If difficulties should arise in a vaginal delivery the fistula may very likely recur; when they have arisen, classical Caesarean section may avoid these difficulties, but it may well be too late to perform this operation safely. The lower segment operation is the operation of choice if labour has been in progress for more than a few hours, and at any time if the membranes have ruptured. But in peeling the bladder from the front of the cervix one may easily tear the scar of the healed fistula, especially if it is adherent to the cervix. But might one attempt vaginal delivery if the fistula had been juxta-urethral, since the lower segment incision will not encroach so far down? Again I think not, because if nevertheless the juxta-urethral fistula should

recur the chances that it can again be repaired are much less than the chances of success for the higher fistula: some 57 per cent in this series as against some 95 per cent. Few of those who have suffered the horrors of a fistula would not share this view and be unwilling to have a Caesarean section; still fewer surgeons who have repaired a fistula would wish to see it subjected to the risks of a vaginal delivery.

It seems justifiable, therefore, to deliver by classical Caesarean section in all cases which one sees before labour begins and when considerations of sepsis do not prohibit. In the majority of cases there will probably be no question of allowing a natural delivery as the cervix and vagina will be too densely scarred.

SUMMARY.

1. Vesicovaginal fistula are classified, according to their situation, as juxta-cervical, midvaginal, or juxta-urethral. In the 40 cases there were 18 juxta-cervical, 5 midvaginal, and 17 juxta-urethral fistulae.

2. The results of their treatment are given, and it is shown that the juxta-cervical and midvaginal fistulae were all operable by the flap-splitting method, and that all but one which were operated upon healed at the first attempt.

By contrast the juxta-urethral fistulae were less successful, only 8 being cured out of 14 cases which submitted to operation.

3. A technique for the flap-splitting operation is described and illustrated, and other operations used and the after-treatment are also described.

4. The view is advanced that the repair by the abdominal route is probably only rarely necessary. It was not required once in this series.

5. It is suggested that transplantation of

the ureters should rarely be required and should be avoided if possible.

6. Classical Caesarean section in suitable circumstances is advocated in cases of pregnancy following a successful repair.

I wish to thank the medical officers who have assisted me, particularly Dr. E. V. Kalyani, M.D., who has helped at most of the operations and taken charge of the after-care in all cases; and Mr. P. M. Ratnasabapathi who has drawn the illustrations.

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Vesicovaginal Fistula

A Review of 42 Cases treated by Plastic Repair or Ureterosigmoidostomy

BY

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THOSE who have seen cases of vesicovaginal fistula all testify to the state of utter misery of the patient. Constantly wet and stinking, she is ashamed to go out and is a nuisance in the house—not only is she objectionable to others but has herself to endure the odour, wetness and resulting soreness. In India she is often deserted by her husband and unwanted in her parents' home. She is unable to support herself except perhaps by begging.

CAUSE.

In countries where vesicovaginal fistula is a common condition the most usual cause is faulty midwifery. Including the cases in this series I have seen altogether about 80. Of these the cause was malignant disease in 3 cases (cervix 2, bladder 1) and 1 occurred after total hysterectomy. In the remainder, that is, about 95 per cent, the cause was obstetrical. Murray and Ahmed¹ in Calcutta found that in 65 inoperable cases the cause in 51 was obstetrical.

But in countries with a good midwifery service the picture changes, and the condition not only becomes a rarity but the cause differs. Operation, especially total hysterectomy, and radium applied to carcinoma of the cervix, are the chief factors. Latzko,² reviewing 97 cases in America over 30 years, finds 65 occurring post-operatively, 28 due to obstetrics and 4 to other causes. Miller³ found 70 per cent in another series to be due to operation.

But, taken as a whole, these postopera-

tive cases are relatively infrequent and the outstanding cause of vesicovaginal fistula is bad obstetrics. Many factors contribute to this cause in a country such as India. In many areas there is a lack of adequate facilities, doctors, nurses, hospitals, ante-natal care. Bad communications make it difficult for a patient to be taken to hospital or for a doctor to reach her home. The Mahommedan religion will not permit a woman to be treated by a man doctor, and this edict is still strictly observed by many millions of Muslims and some Hindu castes. Custom dictates that midwifery be handled by the native "midwives" or *dais*, ignorant women who have learnt their craft from tradition. They are called in when labour begins, do not allow the patient to rest or take nourishment, and insert a dirty hand into the vagina with nearly every pain. Many women, especially primigravidae, become utterly exhausted and are unable to deliver themselves. Their condition deteriorates, the *dais* become alarmed and medical aid is sought so that the responsibility may be shifted. In a typical case one sees an exhausted patient, with the uterus approaching tonic contraction, the head has been showing at the vulva for many hours, and there is a greatly distended bladder. The soft parts have often been abraded.

PATHOLOGY

There is no doubt that in the actual causation of a fistula prolonged pressure of the

head on the soft parts with cutting off of the blood supply and subsequent necrosis is the most important factor, especially if the bladder is distended. In most cases the forceps have to be used to complete delivery, and in some instances careless use and trauma may be contributing causes of the fistula. In such cases the leak of urine may occur at once; but the fact that it usually does not appear till the 3rd or 4th day points to a slow destruction of the vesicovaginal septum by necrosis, and this is more often due to prolonged pressure than sudden trauma. In delivering such cases it is important to perforate the head (the foetus is dead in nearly every case) in order to diminish its size if there is any difficulty, otherwise force in traction may be needed and this should be avoided.

In Africa the custom of female circumcision with resulting scarring which delays delivery is thought by Roberts⁴ to be a cause of fistula, but this is doubted by Preston⁵ who considers delay with pressure to be the most important factor. This custom is unknown among Indian women, and minor degrees of disproportion together with the exhaustion induced by the malpractices of the *dais* lead to the delay which actually causes the fistula.

Prevention will be by improving and increasing the midwifery service, by education and breakdown of superstition and ignorance and by improved roads and transport facilities. In many of the cities of India these conditions already obtain, and thousands of women are safely delivered yearly in the hospitals and nursing homes. The problem for rural India still needs to be tackled.

CASES IN THIS SERIES.

In the five years from March 1938 to March 1943, I treated personally the 42 cases of vesicovaginal fistula now under review. In all these the fistula had occurred

after labour, 33 after the 1st delivery and 9 after 2nd or later deliveries. Some patients were in good condition, others ill-nourished from poverty and various infections. Preliminary treatment was given when necessary, especially for intestinal worms, ascaris and ancylostome, and urinary infection. Most of the patients were young women, half being under 25 (Table I), and in more than two-thirds of the cases when the duration of the fistula could be ascertained, the age at which it had occurred was under 25 (Table II).

TABLE I.
Age of Patient when seen.

| Age | No. of patients. |
|-----------------|------------------|
| 17 to 19 | 7 |
| 20 to 24 | 15 |
| 25 to 29 | 6 |
| 30 | 14 |

TABLE II.
Age of Patient when Fistula Occurred.

| Age | No. of patients. |
|-------------------|------------------|
| 15 to 19 | 10 |
| 20 to 24 | 10 |
| 25 to 29 | 4 |
| 30 | 10 |
| Not stated | 8 |

OBSTETRICAL HISTORY.

In 24 patients a history of the labour was obtained. Three stated that labour had been unduly prolonged, but ended spontaneously, in 12 the labour was terminated instrumentally after much delay, and in 9 there was a history of delivery by the forceps without mention of delay, though it had almost certainly occurred. In 5 cases incontinence of urine had occurred within 24 hours, in 12 cases between the 3rd and 5th days, and in 7

cases later. Two patients had partial control on lying down, but the rest were completely incontinent.

Infection of the bladder was found in 18 cases, in 2 appearing for the first time after operation, the urine not giving any growth on culture beforehand. In all cases *Bact. coli* was present, in 5 gonococcal infection also, and in 2 others the infection was mixed. Eight cases were free from infection throughout. In the remainder (17) a note was not made, but as urinary examination was done as a routine these cases were probably not infected. In all infected or doubtful cases preliminary treatment, usually with sulphonamides, was given.

CONDITION OF VAGINA AND NATURE OF FISTULA.

One patient had a rather lax vagina with a degree of cystocele. In all other cases the vagina was normal in size or narrowed with some degree of scarring. Special note was made of scarring in 11 cases. The size of the hole was pinpoint in 2 cases; small (not more than $\frac{1}{2}$ inch in any diameter) in 8 cases; of medium size ($\frac{1}{2}$ inch plus) in 8 cases; of medium size and at the neck of the bladder in 7 cases; large or very large in 15 cases; and slit-like and situated high up behind the symphysis in 2 cases. In these 2 last cases, and in 7 of those classed as large, the urethra was partially or completely destroyed.

TREATMENT.

A. Plastic Repair.

Most vesicovaginal fistulae can be repaired by plastic methods approaching from the vagina.

The important points in performing the operation are:—

- (1) Preliminary clearing up of infection.
- (2) Excision of scar tissue.
- (3) Mobilization of the bladder wall.
- (4) Closure of the fistula without tension.

(5) Haemostasis.

(6) Drainage of the bladder to prevent over-distension and strain on the repair site.

The fistula had not been present in any case less than 4 months (the ideal time to operate is usually considered to be about 2 months after occurrence), and in some it was of 10 years duration (Table III). Seven patients had been operated on previously in other hospitals, 2 having had 2 operations each.

TABLE III.
Duration of Fistula when first seen.

| Duration | No. of patients |
|-----------------------|-----------------|
| 4 to 6 months | 7 |
| 6 to 12 months | 8 |
| 1 year | 9 |
| 2 to 5 years | 5 |
| 5 to 10 years | 2 |
| Over 10 years | 3 |
| Not stated | 8 |

COMPLICATIONS.

Of the patients 3 had a rectovaginal fistula in addition and 1 a complete tear of the perineum with faecal incontinence.

Technique.

With the patient in the lithotomy position and anaesthetized, the largest possible speculum is placed in the vagina. The labia are retracted and the fistula exposed. An incision is made in the vaginal mucosa encircling the fistula and leaving a narrow rim of scar tissue attached to the bladder wall. The flaps of vaginal mucosa are then dissected upwards and downwards respectively freeing the bladder wall for $\frac{3}{4}$ inch all round. The greatest difficulty may be experienced at the angles of the fistula which may be deep and inaccessible. In such cases it is helpful to extend the incision on to the lateral vaginal walls for it is essential to reach the limits of the fistula.

The edge of the fistula is pared and haemostasis secured, using fine silk ligatures. Interrupted stitches of No. 00 catgut on a small round-bodied needle are then inserted into the bladder wall. These pick up the muscle layer avoiding the mucosa and invert the edges of the fistula. Great care is needed at the angles of the fistula to make the closure water-tight. Finally the vaginal layer is closed with No. 1 catgut. A No. 12 catheter is tied in and continuous drainage of urine maintained. Daily small bladder washes are given. The patient is

Difficulty of approach makes some cases inoperable and this may be due to a very contracted vagina or an inaccessible fistula high up near the cervix in a lateral fornix or behind the symphysis pubis. Some of these cases can be approached by transperitoneal or transvesical routes but of these operations I have not had experience.

Destruction of the urethra is a cause of inoperability, as lack of proper sphincter control leaves the patient incontinent even though the fistula may be repairable.

TABLE IV.

| No. of cases | | Cured | | Improved† | | Failed | | Died* | |
|--------------------|----|-------|----------|-----------|----------|--------|----------|-------|----------|
| | | No. | Per cent | No. | Per cent | No. | Per cent | No. | Per cent |
| 1st Group, 1938-39 | 12 | 5 | 41.7 | 3 | 25 | 3 | 25 | 1 | 8.3 |
| 2nd Group, 1940-43 | 15 | 12 | 80 | 0 | — | 3 | 20 | 0 | — |
| Total | 27 | 17 | 63 | 3 | 11 | 6 | 22 | 1 | 4 |

nursed either prone or supine. The catheter is removed between the 10th and 14th days and the patient encouraged to pass urine frequently. After 2 or 3 days she is allowed to sit up in bed and gets out of bed a few days later.

In all, 27 cases were treated by attempts at plastic repair, being considered operable. The results are shown in Table IV.

These results can be compared with those obtained in the Calcutta Medical College,⁶ when the figures in 104 cases were:—

Cured, 55.8 per cent; failed, 40.4 per cent; died, 3.8 per cent.

CAUSES OF INOPERABILITY AND FAILURE.

Size is not necessarily a contra-indication to operation. Murray and Ahmed¹ state that a pinpoint fistula or one larger than a shilling is inoperable, but most surgeons would disagree with this (Chassar Moir⁷; Scudder⁸). In this series 1 pinpoint fistula out of 2 was cured, and 3 out of the 4 which were at least 1 inch in diameter healed.

Gross destruction of tissue, especially of the bladder wall, prevents repair in a few cases.

Fistulae at the neck of the bladder with the urethra torn away are difficult but may be treated successfully. Earlier attempts at 3 such cases failed, but in the last 3 seen a cure was effected.

TECHNIQUE.

The problem in these cases is that a large hole in the bladder has to be joined to the much smaller urethra. The incision is made as before but an extension in the midline towards the meatus for $\frac{1}{2}$ to $\frac{3}{4}$ inch is added. This allows better exposure of the urethra. Stitches are then inserted to narrow the bladder gap and then approximate the

* The 1 death occurred in a patient who was treated for a month before operation for malaria, ancylostomiasis, anaemia and Bact. coli urinary infection, and who died on the 10th day after operation in a toxæmic state, having had a recurrence of the malaria.

† Partial control in certain positions.

narrowed gap to the urethra. I have found it best to pass these through all the layers of the urethra and then to pick up the bladder-wall, as the stitch often cuts out if one attempts to pick up only the muscle layer of the urethra, and there is loss of valuable tissue when the urethra is already shortened by partial destruction. The sutures closing the lateral extensions of the bladder gap may be interrupted or continuous. The rest of the operation and the postoperative care are as described above.

Much scar tissue, especially in the wall of the bladder, makes healing difficult. If the bladder wall can be mobilized and closed without tension success is likely (Miller,³ Counsellor⁹). It is not necessary to close the vaginal layer (Counsellor⁹) and in 1 case in this series this was quite impossible. However the bladder was mobilized freely and closed in two layers, and the case was cured after a second small operation.

Infection, even though treated before operation, hinders success. Of 11 cases known to be infected and treated by plastic methods, 5 were cured, 5 failed and 1 died (of malaria and toxæmia), while in 16 cases not infected 12 were cured and 4 were failures.

Postoperative hæmorrhage usually spells failure, though 1 of the 3 patients in this series, who had this complication eventually healed. That surgical experience and the acquiring of the necessary technique are important factors in obtaining success is evident from Table IV.

INOPERABLE VESICOVAGINAL FISTULA.

The most effective method of treating inoperable cases is by transplanting the ureters into the large bowel, usually the sigmoid colon. A number of techniques have been devised, some more suited to a 2-stage and some to a 1-stage operation. It is now generally accepted that oblique implantation is the best (Coffey No. 2 technique). Some surgeons consider it better not to leave

anything in the lumen of the ureter (Grey Turner¹⁰), some use fine rubber tubing or a ureteric catheter and others a wick of catgut. More recently Higgins has devised a modification of the Coffey No. 3 technique and Hyams¹¹ has reported favourably on this method for cases of extrophy of bladder but I have not had experience of it.

In this series, 13 cases were treated by ureterosigmoidostomy, 9 in 2 stages and 4 at a single operation. In 6 patients an examination under anaesthesia performed some time earlier confirmed that the case was inoperable: in 7 patients this was not necessary.

In the 9 cases done in 2 stages the ureter was inserted obliquely, with a wick of catgut (No. 00) 1½ inches long left in the lumen. Of these, 6 were cured and 3 died, 1 after the first ureter only had been transplanted. Of the 4 cases treated at one operation, 2 recovered and 2 died. The technique was that used successfully by Sheppard.¹² Thus in the whole series there were 5 deaths in 13 unselected cases, a mortality of 38.5 per cent (cf. Murray and Ahmed,¹ with a mortality of 21.5 per cent in 65 selected cases).

In considering how the operation can be made safer much can be learnt from the cases of failure, and thus avoidable causes of catastrophe may be eliminated. Murray and Ahmed¹ admit that they selected only those patients who were in relatively good health. But it is very urgent to find a technique which can be used with reasonable safety on women whose general condition is not so good, but who implore one to relieve them of their misery. A 2-stage operation is usually safer (Green-Armystage⁶).

INVESTIGATION OF CAUSE OF DEATH.

One of the 5 deaths was due to the anaesthetic (spinal percaine) at the 2nd operation. Another patient developed a urinary-

faecal fistula after the 1st operation, with amoebic dysentery (probably a recurrence of a chronic infection), and after the 2nd operation a retroperitoneal abscess due to leakage at the site of implantation which proved fatal. In this case the wall of the colon was very thin, as is often found in chronic dysentery, and operation was probably contra-indicated. A healthy colon wall seems to be essential.

The 3rd patient died after the 1st operation and postmortem showed that the final continuous suture enfolding the site of transplant had pierced the ureter wall, death being due to urinary peritonitis. This was carelessness in technique.

Of the deaths occurring after a 1-stage operation, 1 was due to renal failure, with anuria and uraemia. This was a case in which a 2-stage operation might have succeeded. The other was a young woman who made a good immediate recovery. She was well until the 16th day and died on the 22nd day after the operation. Death appeared to be due to peritonitis, but permission for postmortem examination even of the abdomen was refused. (I have also performed a postmortem on a patient operated on by another surgeon where death seemed to be due to kinking of the ureter at the site of insertion, with gross dilatation of the ureter and kidney pelvis, and destruction of kidney tissue.)

POSTOPERATIVE COMPLICATIONS.

Of the patients who recovered many had postoperative pyelitis and 1 had anuria with complete suppression for 2 days after the 2nd operation, but eventually recovered. Postoperative distension was troublesome in a number of cases. All the patients except 1 had good control of the rectal sphincter on discharge from hospital, and this last woman passed a few ounces of urine frequently, with sometimes a little leak between.

CONTRA-INDICATIONS TO TRANSPLANTATION OF URETER.

Ureterosigmoidostomy is useless if there is a rectovaginal fistula or a tear of the sphincter muscle of the anus. In these 42 patients 5 had one or other of these conditions. In 1, both fistulae were small and cured at operation. Another was cured of her rectovaginal fistula, but operation on the vesicovaginal fistula at the neck of the bladder failed. One patient had 2 large fistulae, of which the rectal one was successfully repaired after performing colostomy. The vesical fistula was inoperable, and the patient was discharged at her own request to come back later for transplantation of the ureters and closure of the colostomy but she was not seen again.

One patient had a complete tear of the perineum with an inoperable vesicovaginal fistula. When first seen the perineum and anal sphincter were repaired, and a year later both ureters were transplanted at one stage. She had complete control of urine in the rectum. One woman had a large vesicovaginal fistula and a tear of the perineum extending through the sphincter and up the rectum to the level of the cervix. There was great destruction of tissue, and neither bladder nor rectum could be repaired. In this case I first repaired the perineum and anal sphincter (after preliminary colostomy), and at a later stage attempted to close the whole vulval outlet. This procedure creates a "cloaca," making one compartment only of the rectum, vagina and bladder, with one opening, the anus.

This operation was almost successful at the 1st attempt, a small hole admitting a probe being left anteriorly. (The technique of this operation was shown me by my colleague Mr. T. H. Somervill, F.R.C.S., who had successfully treated other patients by this method. In his cases, however, the

anal sphincter had been intact.) This operation is mutilating, but is useful for such cases as these which cannot be relieved by any other means. This patient was a young woman, but had been abandoned by her husband, so that occlusion of the vaginal orifice was not a serious matter. In India there is no remarriage for women. If menstruation occurred, the flow would escape *per rectum*.

SUMMARY.

Vesicovaginal fistula, its causes, prevention and treatment are discussed.

A critical survey is made of the causes of failure in repair, of conditions which make repair impossible; and of the causes of death in patients treated by uretero-sigmoidostomy.

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Peroneal Palsy as a Complication of Parturition

BY

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INTRODUCTION.

This condition was described by von Basedow¹ in 1838, following which the majority of the contributions to the literature came from French obstetricians. A comprehensive study of the available material was published by Hosslin² in 1905, who found that up to date only 81 cases had been recorded. During the last 2 decades, however, this complication of childbirth has received but scant attention from obstetricians; this has tended to give the impression that the condition is one of extreme rarity. Tillman³ in 1935 reviewed the literature to date, collected 107 cases and added 8 more of his own. Recently Barns⁴ reported on 3 cases in this Journal.

The 7 cases here described have been collected from the records of local hospitals over a period of 3 years. Cases 1 and 2 have been under direct personal supervision, Case 3 I saw after delivery and Cases 4, 5, 6 and 7 have been gathered from the records of St. Mary's Hospital, Manchester.

CASE REPORTS.

Case 1, Mrs. E. D., aged 37 years, was a 2nd para who was first seen 1 week before her expected date of delivery. Her previous history was an interesting one. Two years before she had given birth to a living child weighing 9½ pounds. The labour had been extremely difficult, had lasted 36 hours and entailed the application of the forceps. Soon afterwards she had complained of severe pain, numbness and tingling in the left leg and foot, and noticed that she was unable to dorsiflex the left ankle. For the next 5 months she had been bed-

ridden and quite unable to walk, but at the end of the 6th month had improved sufficiently to be able to get about, firstly on crutches and later with the aid of a stick.

During this pregnancy she had been under the care of her own doctor who, knowing the previous history, had decided to induce labour at the 8th month. She had been in a nursing home, but 2 attempts at medical induction had failed.

On examination in hospital the fundus was just below the xiphisternum and the vertex presenting in the right occipito anterior position. The head was high and mobile and there was a first degree of overlap.

The pelvic measurements were as follows:

Interspinous, 9½ inches; intercrural, 11 inches; external conjugate, 7½ inches; diagonal conjugate, 4 inches; intertuberosities, 3½ inches. She had, therefore, a narrow outlet with a narrow sub-pubic angle.

On walking, it was noticed that she dragged her left foot slightly, tending to walk on the ball of the foot. The measurements of the lower limbs were as follows:

Circumference of midthigh, right, 16 inches; left, 15¾ inches. Circumference of midcalf, right, 10½ inches; left, 10¼ inches.

Although these very slight differences are within normal limits it was quite obvious to the naked eye that there was wasting of the anterior tibial group of muscles on the left side.

Movements of all the joints were normal and equal with the exception of dorsiflexion which was weaker on the left side. The other ankle movements of extension, inversion and eversion were unaffected.

The reflexes were brisk and equal and there was no disturbance of sensation. This appeared to be the clinical picture of an almost completely recovered peroneal palsy.

As far as the 2nd confinement was concerned, a 3rd medical induction was successful. Labour progressed satisfactorily until the head was on the perineum when the application of the forceps was necessary. A living child weighing 8 pounds, 8 ounces was delivered without undue difficulty. Following this delivery there were no signs of peripheral nerve damage.

Case 2. Mrs. B. J., age 27 years, had been receiving antenatal care regularly from the 5th month of pregnancy onwards. Her pelvic measurements were as follows:

Interspinous, $8\frac{1}{2}$ inches; intercristal, $9\frac{1}{2}$ inches; external conjugate, $7\frac{1}{2}$ inches; diagonal conjugate, $4\frac{1}{2}$ inches; intertuberos, 4 inches.

One week before term the presentation was a vertex and the position right occipito posterior, with the head still high and mobile. She was admitted to hospital in labour and the head was then just engaging.

The 1st stage was normal, taking $15\frac{1}{2}$ hours. Good 2nd stage pains commenced but after 3 hours there was no further advance of the head and no attempt at rotation. It was therefore decided to perform a manual rotation and forceps-extraction. The head was rotated with some difficulty and Neville-Barnes forceps applied. The blades slipped in easily and seemed to fit snugly—there was no necessity to reapply them. Traction was then applied in the usual manner but considerable force was necessary to produce any advance. The pull was a steady one, the blades did not show any signs of slipping and the vertex was delivered strictly in the antero-posterior position. A still-born child weighing 9 pounds was extracted.

The following day the patient complained of pain, numbness and tingling over the outer aspect of the left thigh and the whole of the leg and foot. On examination it was noted that full-dorsiflexion could not be obtained although there was no true foot-drop. Over the dorsum of the foot there was a diminution of epicritic sensation—this corresponding to the area where the paraesthesia was most marked. The symptoms gradually improved and by the 6th day she had regained full dorsiflexion and all the disturbances of sensation had disappeared. This sequence of events indicated a mild transient peroneal palsy.

Case 3. Mrs. R., age 20 years, was a primigravida who went into labour spontaneously at term and was delivered at home by her own medical attendant. The history was that she had been in labour for 2 days, the foetal presentation being a vertex in the right occipito posterior position. A manual rotation to a right occipito anterior position and forceps-extraction was performed. This was said to have been difficult and resulted in the delivery of a stillborn child of moderate size. The weight was not recorded. I saw her 10 weeks after delivery. Her external measurements were as follows:

Interspinous, $8\frac{3}{4}$ inches; intercristal, $9\frac{3}{4}$ inches; external conjugate, 7 inches; diagonal conjugate, $4\frac{1}{2}$ inches; intertuberos, 4 inches.

On examination she limped badly, lifting her left leg in an exaggerated manner in order to clear the left toe from the ground. No obvious wasting was seen. There was a marked difference in skin temperature, the left leg being much colder and paler in colour. Movements showed that she had a complete loss of eversion and extension of the ankle joint. Sensation was normal to pinprick and cotton wool. The patient did not now experience any tingling in the leg but this had been marked over the outer aspect of the ankle for a few weeks following delivery. She was referred to an orthopaedic surgeon for treatment.

Case 4. Mrs. A. C., aged 34 years, a primigravida, had marked bowing of the long bones although there was no history of rickets. Her pelvic measurements were as follows:

Interspinous, $10\frac{1}{4}$ inches; intercristal, $11\frac{1}{4}$ inches; external conjugate, 8 inches; diagonal conjugate, over $4\frac{1}{2}$ inches; intertuberos, 4 inches.

She was admitted to hospital in labour with head in left occipito anterior position and going into the pelvis.

She had a long 1st stage taking 77 hours and then, as good 2nd-stage pains lasting 2 hours had not caused the head to advance, the obstetrician in charge carried out a mid-forceps extraction. Neville-Barnes forceps were used and the delivery was exceedingly difficult. A living child weighing 8 pounds 2 ounces was extracted.

Later the patient complained of some pain in the right leg, and the following were found: There was a paresis of the anterior tibial and peroneal

muscles of the right leg with a consequent foot-drop and the power of dorsiflexion was very weak. With massage and rest in the "anatomical" position there was a definite improvement but the foot-drop was still present when she was discharged from hospital. She was referred to an orthopaedic clinic for further treatment.

Case 5. Mrs. E. F., aged 38 years, had had 5 normal deliveries previously, the largest baby weighing 7 pounds. Her pelvic measurements were unfortunately not recorded in the notes. She was admitted to hospital as an emergency case, after being in labour for 44 hours—the membranes had been ruptured for 7 hours. She had had 4 vaginal examinations before admission and when seen in hospital the uterus was found to be at term with the head past the brim. Further vaginal examination showed the presentation to be a brow in the left frontal anterior position and the os was almost fully dilated. Under general anaesthesia attempts were made to convert the presentation to a vertex or failing that to a face, but the presenting part was so firmly fixed that all such attempts were of no avail.

The obstetrician thereupon performed a craniotomy and a dead foetus weighing 6 pounds 11 ounces was extracted. Two days later the patient complained of pain in the right leg and examination showed that she had weakness of dorsiflexion in the right ankle. The reflexes were normal and there was no disturbance of sensation. She was treated by massage and passive movements, and on discharge the function of the ankle had returned almost to normal.

Case 6. Mrs. C. C., aged 21 years, was a primigravida who had been receiving care at a municipal clinic. A few days before the expected date of delivery she was seen by the obstetrician in charge, who found that the vertex was still mobile and was presenting in the right occipito posterior position. It was decided that she should be confined in hospital. Her measurements were as follows:

Interspinous, $9\frac{3}{4}$ inches; intercrisal, 10 inches; external conjugate, 8 inches; diagonal conjugate, over $4\frac{1}{2}$ inches; intertuberos, 4 inches.

She went into labour spontaneously 1 week after the expected date of delivery. Some 15 hours afterwards the cervix was fully dilated, the head

had made no attempt to rotate and the foetus was becoming distressed. A manual rotation was performed and Milne-Murray axis traction forceps applied. A living child weighing 8 pounds 3 ounces was extracted with considerable difficulty. The following day she complained of cramp-like pain in the left leg and shortly afterwards it was noticed that she was quite unable to dorsiflex or evert the ankle. On examination no sensory loss was detected. She was treated by rest in a right-angled splint and later by massage. Three weeks after delivery she still had an almost complete paralysis of the dorsiflexors of the left foot. The dorsiflexors of the toes were acting well. The invertors and evertors were acting poorly. Plantar flexion was strong. There was no sensory disturbance. She was referred to an orthopaedic clinic and lost sight of by the hospital.

Case 7. Mrs. L. G., aged 35 years, was a case of toxæmia of pregnancy occurring in a primigravida. She was referred to the hospital by her own doctor a month before the expected date of delivery as she had albuminuria and was vomiting persistently. The foetal head was beginning to engage in the left occipito posterior position. Her measurements were as follows:

Interspinous, 10 inches; intercrisal $11\frac{1}{2}$ inches; external conjugate, $7\frac{3}{4}$ inches; diagonal conjugate, over $4\frac{1}{2}$ inches; intertuberos, 4 inches.

She was treated for the toxæmia by a low protein diet and rest, etc., but 14 days later albumin was still present in the urine and it was decided that labour should be induced. A Drew-Smythe catheter was used to rupture the membranes. Labour commenced and the vertex descended into the pelvis in the left occipito posterior position. The occiput made an attempt to rotate forwards and the 2nd stage was delayed with the head transversely fixed. There was some maternal distress and interference was indicated. With some difficulty the vertex was disengaged and rotated manually to the left occipito anterior position, the forceps applied and a living child extracted.

The following day the patient noticed tingling in the right lower limb and found that she was unable to dorsiflex or evert the right ankle. On examination it was found that she had a right peroneal palsy with no sensory loss. A right-angled splint

was applied and daily massage carried out. She went home 14 days after delivery and was referred to an orthopaedic clinic where massage and electrical stimulation were ordered. She was seen 1 month later and had improved considerably but still had a slight degree of paralysis. She failed to report again for further examination.

COMMENTARY.

Kleinberg³ maintains that 1 or more of 3 essential factors are always present in this complication of childbirth. These are:

- (a) Disproportion.
- (b) Prolonged or difficult labour.
- (c) Instrumentation.

The vast majority of cases reported do bear this out, but there are records in the literature of peroneal palsy after normal deliveries. The object of this paper is to attempt to correlate the position of the foetus with the side on which the paralysis occurs, in order to determine whether injury could be due to direct pressure on the sacral plexus or not.

It is easy to understand that with the greater diameter of the head lying in one or other oblique diameter of the superior strait of the pelvis, any adverse relation between these two dimensions might result in pressure on the sacral plexus (Hünemann 1892⁶). It is perhaps less easy to understand the vulnerability of the peroneal nerve component of that plexus—the subject of this commentary. The most likely reason can be based on pure anatomical data.

The peroneal nerve supplies the dorsal aspect of the lower limb (using the term dorsal in an embryological sense) and therefore arises from the posterior aspect of the sacral plexus. Thomas⁷ writes "The upper roots of the sacral plexus do not lie on the pyriformis muscle but against the bony walls of the pelvis and are thus exposed to pressure during certain difficult labours. Dorsal offshoots of these nerves

lie against the bone and receive the chief injury. The external popliteal nerve is made up of these fibres and therefore paralysis is chiefly located in the distribution of this nerve."

Thus the main mass of the sacral plexus is to some extent cushioned by the pyriformis, whereas the peroneal elements are devoid of any such protection. Linden⁸ states that the condition must be rare in the flat non-rachitic or rachitic pelvis as the plexus is protected against pressure from the foetal head on account of the 2 deep niches on either side of the projecting vertebral promontory. On the other hand, in a generally contracted pelvis the paravertebral grooves are much shallower and place the plexus in a much more vulnerable position.

In Case 1 of the above series the presentation at the first pregnancy (when the damage was done) is not recorded. In the remaining 6 cases the presentations were as follows:

| Case | Presentation | Side of palsy |
|------|--------------------------|---------------|
| 2 | Right occipito posterior | Left |
| 3 | Right occipito posterior | Left |
| 4 | Left occipito anterior | Right |
| 5 | Left frontal anterior | Right |
| 6 | Right occipito posterior | Left |
| 7 | Left occipito posterior | Right |

In Cases 2, 3, 4, 5 and 6 the foetal head occupied the right oblique diameter of the pelvic inlet, therefore if direct pressure of the foetal head on the nerve were to occur the palsy should be a right-sided one. This was true in the left occipito anterior and left frontal anterior (Cases 4 and 5) but not in the right occipito posterior cases. Similarly in Case 7, the paralysis is on the opposite side to the diameter occupied by the foetal head. One can reasonably conclude that trauma due to foetal head pressure may be responsible in 2 of the 6

cases. It may also explain the cause of the paralysis in non-instrumental deliveries.

In order to explain the other 4 cases, however, one must presume that the peroneal nerve has been damaged by instrumentation.

SUMMARY AND CONCLUSIONS.

1. Seven cases of peroneal palsy are recorded—3 from personal observation and 4 from hospital records.

2. These cases bear out the following points:

(a) The palsy follows difficult deliveries which entail extraction by the forceps.

(b) The paralysis is unilateral.

(c) It occurs on the side opposite to the one occupied by the greatest diameter of the foetal skull in the majority of cases.

(d) The cause in the majority of cases must be instrumentation. In the minority direct pressure of the foetal head may be the cause, though in these, too, instrumentation cannot be excluded.

(e) Pain and paraesthesia, though transient and not severe, precede the paralysis.

(f) The paralysis affects the dorsiflexors and evertors of the ankle.

(g) The paralysis will, in the majority of cases, clear up, and in those in which permanent damage is done the final paralysis is considerably less than the initial loss of function.

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My thanks are due to Sir William Fletcher Shaw, Dr. F. H. Lacey and Dr. R. Newton for their kind permission to report cases. I am very grateful to Professor D. Dougal and Dr. C. P. Brentnall for their case records and also for their helpful criticism.

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ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS.

The following have been elected to the Fellowship of the College :

Geoffrey Shedden Adam.
Caroline Anne Elliott.
Eric Arthur Gerrard.
Arthur Machen Hill.
John Joseph Kearney.
Robert James Kellar.
Alice Meave Kenny.
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Bruce Toomba Mayes.
Herbert Kenneth Pacey.
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Frederick Ross Stansfield.
Geoffrey Ashburton Thompson.

The following have been awarded the Diploma of the College :

Isabel Helen Mary Blyth.
James Taylor Carson.
Horatio Jose Antonio Conte-Mendoza.
George Kenneth Emsley.
John Lumsden Farmer.
Julius Juel Handler.
Denzil Heap.
Alistair Henderson.
Michael Hutchinson.
William Johnston.
Edward Ellis Jones.
Kathleen Lawrence.
Betty Jean Poland.
David Bradshaw Stewart.

"Gas and Air Analgesia," second edition. By R. J. Minnitt, M.D. (Liverpool), D.A. (R.C.P. and S. Eng.). Ballière, Tindall and Cox.

THIS is a small book written primarily for those interested in the relief of pain during labour, but a short chapter is devoted to showing this usefulness in the field of minor surgery. An appealing feature of the book is the obvious aim of the author to spare no effort in yet further improving upon present achievements, and this is particularly well brought out in the opening chapter which gives a short and interesting account of the evolution of gas and air analgesia.

The descriptions of the apparatus in its various forms, and the principles embodied, are clear and very well illustrated. Much space is wisely devoted to describing the apparatus in actual use upon the patient as the success of gas-air analgesia depends—and this is probably not fully realized by many—upon attention being paid to certain details. To stress this, commonly made mistakes are shown. A new technique, claimed to be a big advance on its predecessor, is described for giving better analgesia during the 2nd stage.

More space might have been devoted to the use of anaesthetic drugs with the gas-air analgesia apparatus. One is left wondering for what types of case this form of analgesia may be recommended—if, indeed, it may be safely employed in obstetrics at all, e.g., for the head sweeping over the perineum, or for repairing a torn perineum. The statement "the mother's pulse and foetal heart should be estimated hourly" is, however, a somewhat more serious fault: the foetal heart during the 2nd stage of labour (when the apparatus is more often in use) should, of course, be auscultated very much more frequently.

Apart from such minor faults this is an excellent little book which should be read by all—doctors, midwives and students alike—who practise obstetrics.

"Midwifery for Nurses," ninth edition. By Hendry Russell Andrews, M.D., B.S. (Lond.), F.R.C.P. (Lond.), F.R.C.O.G., and Victor Lack, M.B., B.S. (Lond.), F.R.C.P., F.R.C.S. (Edin.), F.R.C.O.G. Edward Arnold and Co.

THIS is, on the whole, a disappointing book. The illustrations, it is true, are good and particularly so in the case of that complex structure, the foetal circulation. Certain sections notably those dealing with abortion, normal and abnormal labour including the various mechanisms, are dealt with in a manner that warrants little criticism—though it is somewhat disconcerting to read that the doctor need be notified in a breech case in labour only if the legs, on vaginal examination, are found to be extended.

It is disappointing to find no mention of a blood-transfusion service (employing bank blood). Thus the nurse is advised in a case of severe antepartum haemorrhage when the doctor is delayed to send, on her own responsibility, the patient to hospital in an ambulance. Surely it would be wiser counsel to raise the lower end of the bed and inform, by telephone, the nearest maternity hospital so that an experienced member of the staff might proceed to the patient with all necessary equipment (blood-transfusion apparatus, etc.). It is even more reprehensible to advise the nurse, in a case of severe postpartum haemorrhage when the doctor is not present to undertake manual removal of the placenta with the patient in extremis (as an anaesthetic would not be required in such a case). An experienced and capable obstetrician would not undertake such a procedure nowadays without a preliminary blood-transfusion.

In dealing with the late toxæmias of pregnancy, too much stress is laid upon albuminuria and too little upon the blood-pressure changes. Further, whereas chronic nephritis—a rather rare comitant of pregnancy—is specially mentioned as predisposing to late toxæmia, not a word is

mentioned of essential hypertension—a condition much more often associated with pregnancy and one which certainly favours late toxæmia.

A correct sense of proportion is totally lacking in many places. Thus the bogey of locked twins is unearthed, an unnecessarily large amount of space is devoted to insanity and to that extreme rarity, acute inversion of the uterus. One finds more space given to the admittedly interesting but actually unimportant condition known as pseudocyesis than to such an important and topical subject as diet during pregnancy. The space mispent in describing rarities should have been devoted to more profitable subjects. To give one example: prolapse should be mentioned as a very common late complication of labour which might be averted by properly performed exercises designed to strengthen the pelvic floor, and that it is the duty of the nurse in attendance during the puerperium to see that the patient carries them out. Naturally, a detailed account of one or two of these exercises should be presented to the reader.

In a book whose authors state that a principal aim has been to keep it as short as possible it is pointless and quite confusing to describe a similar condition in one place under the heading "flushed breast," and in another place under the heading "mastitis, or inflammation of the breast."

The chapters devoted to the infant are, on the whole, satisfactory, though mention might have been made when dealing with breast-feeding as to whether one or both breasts should be employed at each feed. On the other hand, the very scant reference to the problem of prematurity is a serious fault. Why, in the brief account that is given of the management of the premature baby, is no mention made of its admission as early as possible to a special nursery where life-saving facilities (oxygen, etc.) are available? Perhaps the defeatist attitude of the authors in their statement "it is unlikely that an infant of less than 32 weeks will live more than a few days" provides the answer.

In short, this is a book which, in its present form, I should hesitate to recommend to pupil-midwives.

"A Handbook of Gynaecology" for the Student and General Practitioner. By BETHEL SOLOMONS, B.A., M.D., F.R.C.P.I., 4th Edition. Baillière, Tindall and Cox.

THIS is a "cram-book" rather than a "hand-

book," and despite the fact that the preface states that the book has been written primarily to aid the student and general practitioner in his practical work and not to satisfy specialist needs, this is hardly the case. What justification is there for discussing, in some detail, the division of the cervix as a line of treatment in the chapters on Dysmenorrhoea and Sterility? The statement that the student must know about this operation for examinations is surely untrue, and furthermore can only do harm. If the student is led to believe he must know of this rarely-performed operation, he may well burden his mind with all the other rarities mentioned.

Another major fault is the listing of conditions under various heads, with little or no attempt to assist the student or practitioner in assessing their relative importance. Thus in a list of local uterine causes for dysmenorrhoea, an extreme rarity, viz., atresia of the cervix, is sandwiched between two much more commonly found conditions, viz., acute antelexion and hypoplasia. The introductory remarks to the symptomatology of fibroid uterus are even more remarkable: the reader is informed that the patient may suffer from severe toxic symptoms—which are dealt with in some detail—before any mention is made of the much more common symptoms. Again, although the "safe period" is discussed at great length it is disappointing to find that no mention of other forms of contraception is made: yet every general practitioner should have knowledge of them and be able to impart it to those couples who desire it.

While certain chapters, such as that of the routine examination of the patient and that of ectopic gestation, are written in an interesting and instructive way, the majority are written too concisely and contain such innumerable headings, divisions and sub-divisions—presumably to ensure that no point, however unimportant, is omitted—that by their very completeness they become distinctly boring. The concluding chapter by Dr. Chance dealing with X-rays and Radium in gynaecology is given in a most lucid and comprehensive way and deserves special mention.

For a book of its size too much space is devoted to operative gynaecology. Most will agree that the student should have some knowledge of common operations such as prolapse, but it seems point-

less to describe highly specialized types of operation, such as salpingostomy, in detail. It is surprising to find no mention of intravenous administration of glucose-saline in the treatment of post-operative ileus. Again, in the treatment of collapse following post-operative haemorrhage, one would have thought that blood-transfusion (employing bank blood) would have ranked more

important than giving the patient plenty of hot drinks.

To sum up, this book has obviously been written from the examination standpoint. It will appeal to those students who like the facts presented in tablet form, but will be less appealing to the more thoughtful student and particularly to the general practitioner.

J. F. B. WYPER.

REVIEWS OF HOSPITAL REPORTS

REPORT OF THE GLASGOW ROYAL MATERNITY AND WOMEN'S HOSPITAL FOR 1943.

The Medical Report of the Glasgow Royal Maternity and Women's Hospital for the year 1943 follows its customary form. It is a most comprehensive publication. In the preface the general plan of the hospital service is outlined. There are 174 beds—73 antenatal, 75 lying-in, 15 for abortions, and 11 for isolation. In addition there are two labour wards with 9 and 6 beds respectively: in the isolation block there is a labour room with 1 bed. The hospital is divided into three units. The isolation wards are quite separate from these units. Frankly septic cases are removed from the hospital altogether to the isolation hospitals of the local authority.

Patients are mainly (85.5 per cent) drawn from the city of Glasgow. The remainder come from outlying districts which have no adequate hospital facilities; some of these are remote. Sixty-eight per cent of all admissions were considered abnormal. There were 4,794 admissions of which 3,361 resulted in deliveries. Being a large hospital the numbers are necessarily large. In a report this is an advantage for the statistical matter presented is less likely to be deceptive when reduced to percentages than is the case with smaller numbers.

In each section the condition under review is presented in varying degree of detail for the year concerned. Then follows a condensed tabular survey of the results of the previous five-year period. This latter is a valuable, if uncommon, feature.

Malpresentations are set out with single case data except in the case of breech presentation. Of particular interest in breech presentations are the results of the uncomplicated breech in primigravidae. (It would be helpful if the term uncomplicated were defined). There were 55 cases of uncomplicated primigravid breech. There were no maternal deaths, but 11 babies were stillborn, and 5 died. The foetal mortality is therefore 29 per cent. Prolapsed cord and cord presentation

continue to exact the usual high toll of foetal life, 71.7 per cent of 46 cases. Of the 13 children which survived 3 were born spontaneously (as vertex presumably), 4 as breech presentations, 5 as breech following internal version, and 1 by the forceps. To a reader, attempting to assess the value of different lines of treatment, it would be helpful to know the degree of cervical dilatation when the condition was first diagnosed, but in no case is this stated.

Obstetric operations are classified and tabulated clearly. Some errors creep in, e.g., on page 30 we are told that labour was induced by artificial rupture of the membranes in 17 cases of contracted pelvis and on page 38 in 21 cases. The defining of 2nd stage delay (page 27) is erroneous and requires revision. Contracted pelvis and disproportion receive considerable attention, and merit careful study. Antepartum haemorrhages and the hypertensive toxæmias are set out case by case. In the accidental haemorrhage tables "first bleeding before delivery" is a heading. This might well be introduced into placenta praevia tables, if only to emphasize the importance of the "warning" haemorrhage. Similarly the "recording of symptoms and duration in days" (oedema, headaches, etc.) in the hypertensive toxæmias is valuable. It might be useful to add the nature of the earliest symptom or sign observed with the period of gestation at which it was first noted.

Perhaps the most outstanding feature of the whole report is the section dealing with maternal deaths. Factors sometimes overlooked are significant in the consideration of the numerical death-rate in any hospital. The number of maternal deaths in the whole area served by the hospital is obviously of importance, as also is the standard of practice in the antenatal clinics and of the practitioners in the district. Other factors too, the percentage of women who seek antenatal care, the standard of living of the community, may influence the hospital figures as do the more obvious facts such as the proportion of emergency to booked cases. While this is so 80 maternal deaths is a rather disquieting number. Viewed another way

it means that 1 woman dies in the hospital every 4.5 days. The causes of death are tabulated. One patient was not pregnant. Reviewing the details of the other 79 deaths, some emergencies had had antenatal care, or none at all, only to die of hypertensive toxæmia. Some 15 patients died of postpartum hæmorrhage. Of these 10 arrived in the hospital "shocked," "collapsed" or even showing "air hunger." If the transfer of a patient from her home to hospital means that her chance of recovery is thereby to be prejudiced, obviously the hospital service should be taken to the patient. One illustrative case will suffice.

"3257. Previous history, nothing of note. Obstetric history, three previous full-time spontaneous deliveries. Patient had had no antenatal care. Labour commenced at 1 a.m. on August 31st, 1943, and the district staff were sent for at 5.15 p.m. Hydramnios was diagnosed. A mature, normal child was delivered spontaneously at 8.40 p.m.; 10 minutes later the patient suffered a 3rd stage hæmorrhage and lost 2 to 3 pints of blood. The district resident was called out and saw the patient, who was extremely restless and was bathed in a cold sweat. The placenta was retained. Morphine gr. $\frac{1}{4}$ and pituitrin $\frac{1}{2}$ c.cm. were given. On admission the patient *was in much the same state as when first seen but for slight air hunger* (italics mine). A plasma transfusion was immediately commenced and the condition of the patient improved thereafter. An unsuccessful attempt to express the placenta was then made and her condition deteriorated. One pint of blood was then transfused, but she died in the course of the transfusion. Post-mortem not granted."

There is no mention in the report of the arrangements to cope with this kind of emergency. The value of an obstetrical "flying squad" is well known. An essential part of that team is an obstetrician of considerable experience: a house-surgeon whose obstetric experience varies between 3 and 6 months cannot be expected to have the clinical judgment necessary to deal with such a case entirely on his own. Expert preliminary treatment in the patient's home before she is removed to hospital may make all the difference between life and death. If the hospital does not have such a scheme the creation of one might well be considered.

Of 257 patients subjected to Caesarean section 11

died (4 per cent). In the Caesarean section tables we are not told, except when done for contracted pelvis, whether the patients were in labour, which were repeat sections, nor the type of anaesthesia used. Of these 11, 3 died of peritonitis, 1 of paralytic ileus, 1 of (spinal) anaesthesia, 1 of postpartum hæmorrhage and the remainder from a variety of causes. There is fairly prevalent to-day the opinion that the mortality from Caesarean section, as a whole is 1 per cent. It has been suggested in the Royal Society of Medicine that, as the mortality has been reduced to 1 per cent, we should concentrate now on reducing its morbidity. Let us keep in mind Professor Claye's suggestion (*Proc. Roy. Soc. Med.*, 1943, xxxvi, 528), to institute a country-wide inquiry into Caesarean section. The lower segment operation, the ever widening indications, the free use of blood transfusion and chemotherapy have had a profound influence upon obstetric practice. The time is approaching when it will be possible, as it is now desirable, to institute this inquiry. What is the death-rate from Caesarean section to-day? It is said to be 1 per cent. Is it?

A tabular analysis of stillbirth (95/1000 viable births) and neonatal deaths (61/1000 live births), puerperal fever and puerperal pyrexia bring the year's report to a close. There is finally an appendix which gives a resumé of the hospital statistics for the past 10 years.

REPORT OF THE SIMPSON MEMORIAL MATERNITY PAVILION, ROYAL INFIRMARY, EDINBURGH, FOR 1943.

The Medical and Clinical Report of the Simpson Memorial Maternity Pavilion, Royal Infirmary, Edinburgh, for the year 1943 concerns 3,760 patients treated in the hospital and 784 treated in their own homes. The report is devoted mainly to the in-patient side of the obstetric service, but contains a brief summary of the cases delivered at home. There is also an extensive paediatric section.

The in-patient maternal section opens with a summary of mortality and morbidity. Then follow summaries of the usual complications of pregnancy and labour. These summaries are mainly tabular, headed in some cases by a brief explanatory statement or synopsis. In the case of breech

presentation, contracted pelvis, eclampsia, embryotomy and placenta praevia single-case data are given in more extensive additional tables. Three pages are devoted to short notes on maternal deaths. An interesting comparative table of the main features of this 1943 report and of that of each year back to 1930 is included.

There were 14 maternal deaths (one of these died undelivered) in the hospital and 2 patients died after being transferred to the City Fever Hospital, making 16 deaths in all. The total maternal mortality of the 3,760 in-patients is therefore stated as 0.42 per cent. If calculated in relation to live-births (to make it comparable to the national figure) there would be 16 maternal deaths for 2,754 live-births, i.e. 0.58 per cent. Some of the notes on these maternal deaths are just too short. One (booked) case (2410/43) of placenta praevia was treated by classical Caesarean section. "Death occurred immediately after the operation from severe postpartum haemorrhage. No autopsy." The presumption is that she was in a good state at the start of the operation. Was the uterus flabby all the time after extraction of the child? Did the surgeon have to consider whether hysterectomy was called for or not? Did this severe postpartum haemorrhage occur quite unexpectedly immediately after the operation was complete? What anaesthetic was used? We are not told. Another (booked) case 3,076/43 was considered to be normal until she had a third-stage haemorrhage which was treated by expression of the placenta and blood transfusion. Local uterine sepsis developed and, on the ninth day, secondary postpartum haemorrhage occurred requiring further transfusion. Intermittent haemorrhage recurred for another six days. The uterus was then explored and two small pieces of placenta were obtained. "Bleeding continued through the intra-uterine pack, and did not stop *even when this was repeated twice during the same day* (italics mine), so that ultimately subtotal hysterectomy was performed with continuous transfusion, but death occurred shortly afterwards. No autopsy." When was the pack first introduced—at the time when the two pieces of placenta were removed? Was it introduced first under anaesthesia? Were the repeat intra-uterine packings performed under anaesthesia? Did she have four general anaesthetics in one day? We are not told. The same lack of full information is tantalising in

the summarized tables of the complications of pregnancy and labour. This is seen, for example, in the details given under Adherent and Retained Placenta. The placenta was expressed 24 times. Under anaesthesia? We are not told. The placenta was removed manually 31 times. Of these 55 patients 18 required blood transfusion, 32 had some degree of third-stage haemorrhage, while 33 were not admitted to the hospital until after the birth of the child. There is no means of telling, however, which patients required the blood transfusions. There were 18 cases of "failed forceps outside." The treatment in hospital was by expectancy resulting in spontaneous delivery, forceps, craniotomy, or Caesarean section: there was not one maternal death. But we are not told why the forceps had failed previously, whether the cervix was fully dilated on admission or whether there was any maternal morbidity following the successful treatment. I have stressed this aspect deliberately because by published results the trend of obstetric thought and practice is guided and influenced. Much time is spent and much labour expended in producing valuable reports such as this. But if they do not provide sufficient information for profitable study then, in measure, they fail in their purpose.

The sections set out with single-case data contain much of interest. There were 55 cases of uncomplicated primigravid breech delivery, resulting in 1 still-birth and 3 neonatal deaths (7.2 per cent foetal mortality). When twins, or one foetus of a twin pregnancy, are born by the breech "complicated" breech would seem the normal classification. Here they are included in the "uncomplicated" table. In this case the foetal mortality figure, however, is not materially altered by their inclusion.

The paediatric section is comprehensive. It is based on the infants born during the year, whereas the obstetric section is based on the admissions for the year. Neonatal mortality and morbidity are tabulated in some detail. Three deaths occurred in infants over 1 month old. The neonatal death-rate was 198 per 1,000 viable births for premature (viable) infants, 14.7 per 1,000 viable births for mature infants and 30.9 per 1,000 for all infants. No previsible (under 2¼ lbs.) child survived. In fact none less than 3 lbs. in weight survived.

At the end of two weeks or previous discharge 83.3 per cent of infants were wholly breast fed, 5.9

per cent were breast fed with complementary feedings and 10.8 per cent fed entirely artificially. The causes of death have been investigated fully. Out of 108 deaths there were 101 autopsies. Of 143 stillbirths the cause was known in 64—determined by postmortem examination in 61 and by evident congenital defect in 3. The neonatal deaths and stillbirths are correlated with the normal and abnormal pregnancies of the mothers. Figures of the postnatal infant welfare attendances bring the report to a close.

THE SIXTH REPORT FROM THE DEPARTMENT OF OBSTETRICS AND GYNAECOLOGY IN THE UNIVERSITY OF OTAGO.

JULY 1942 TO JUNE 1944 INCLUSIVE.

The work was carried out in the Queen Mary Maternity Hospital, Dunedin. The students here each deliver 4 patients and witness the delivery of a further 20. After this each must deliver another 16 patients. This is an improvement of the minimal requirements for medical students in British Schools.

During these 2 years, exactly 1,000 women were delivered of 1,016 children, 16 of the patients having twins. The report makes pleasant reading. It might even be said to have a note of cheerfulness. Here we see midwifery as almost a physiological process, although occasionally something goes wrong. Only 73 of the patients delivered were admitted as emergencies; the other 927 all received antenatal supervision from members of the hospital staff.

There were 60 cases of toxæmia or hypertension. Some of these were severe, but the incidence of toxæmia on the whole is low. As far as can be judged the standard of blood-pressure adopted for hypertension is 140 systolic or 90 diastolic. At any rate one case is included with blood-pressure 150/80 and no other symptoms or signs. Of these 60, 4 had eclampsia—a fairly high incidence. No toxæmic patient died. There were 9 stillbirths and 2 neonatal deaths.

Malpresentation occurred 74 times, 34 as persistent occipito-posterior position, 2 as transverse lie, 3 as face and 35 as breech presentation. In the latter it is not possible to calculate the foetal

mortality in uncomplicated deliveries, but as there are 35 breech deliveries in this group it is not of the type of anaesthesia instance. Of the 35 breech deliveries 11 were born at full-time as were also 35. The remainder from the Caesarean section table were in labour, when done for contracture of the peritonitis, 1 of post-maturity.

Delivery was effected by the forceps in 8.8 per cent, with 1 maternal death. The Caesarean section was carried out 29 times. This has been suggested that, as 29 per cent of the emergency cases were delivered by Caesarean section while only 1.4 per cent of the non-emergency cases required the operation. It was indicated that, as 29 per cent of the emergency cases required the operation, 3 for central placenta praevia, 2 for uterine fibroids and the remainder for a variety of indications. The lower segment Caesarean operation was done 22 times and the classical 7 times without a maternal death. Only 3 cases were morbid, 2 because of stitch abscess and 1 from thrombo-phlebitis. Three Caesarean babies were stillborn, the indication for these sections being eclampsia, accidental haemorrhage, and disproportion, with foetal distress. There were 32 cases of antepartum haemorrhage of which 12 were due to placenta praevia. Of the 9 cases of placenta praevia which did not require section, 2 were treated by Willett's forceps, 4 by puncture of the membranes while treatment was not required in the remainder. Postpartum haemorrhage occurred 7 times with 1 death. Hysterectomy proved necessary because of placenta accreta in 1 case in which delivery had been by the forceps. This case is also included among 28 cases of retained membranes (p. 14) which should probably read retained placenta.

There were 2 maternal deaths. Both occurred from shock following operative delivery. The first had haemorrhage from placenta praevia, manual rotation of the head and forceps delivery: postpartum haemorrhage necessitated manual removal of the placenta. In the other fatal case difficult manual breech delivery resulted in a complete tear. Death from shock followed 1 hour after delivery and repair. In the maternal morbidity table these 2 deaths appear to have been omitted. While recognizing that, the incidence of morbidity is very low. On the B.M.A. standard 10 cases occurred. In two years there was not one case of notifiable puerperal sepsis—a truly remarkable achievement.

Infantile mortality and morbidity are reviewed

nts born at full time 13 were still-natal deaths occurred. The figures on (p. 20), however, do not add up of 93 premature infants 15 were still-lies.

The same 2 years there were 1,208 cases in gynaecological wards. There were 11 deaths in 5 were post-operative, 3 because of uterine carcinoma, and 3 from post-abortion.

It would have been interesting to have had details about the post-abortion deaths, but none is given. Once again the low incidence of these conditions is striking, e.g., there were only 2 cases of acute salpingitis, and 15 cases of sterility—in 2 years! Chronic cervicitis and downward displacements of the genital tract show a more normal frequency. Neoplasms both benign and

malignant are found in customary frequency. Professor Dawson and his staff must be proud of these results for they are excellent. While in no way detracting from their achievement certain facts seem to emerge from this report. Their patients are no more immune to neoplasms, malignant or benign, or to the remote sequelae of obstetric injury than the average hospital patient. But they do appear to enjoy relative immunity to contracted pelvis, toxæmia of pregnancy, placenta prævia, puerperal infections and later pelvic infections and also perhaps sterility. It prompts the question of how far are climate, high standard of housing and food, economic and financial security responsible for the better results among these patients than among their less fortunate sisters at home.

ANTHONY W. PURDIE.

INDEX TO CURRENT LITERATURE

In this Index an endeavour will be made, so far as war conditions permit, to maintain an up-to-date record of all titles bearing on obstetrics and gynaecology and the infant. The classification aims at making immediately available for the reader the titles under the various subject headings. In the majority of instances the title is obtained from the original publication. Where this has been impossible, the title has been obtained from the abstracting journal shown in brackets. Reprints will be welcomed and should be sent to the Editor.

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NEW SERIES

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Placenta Praevia—A Study of 174 Cases

BY

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IN the year 1937 the Honorary Medical Staff of the Royal Maternity Hospital, Belfast, decided to allocate the treatment of the 3 common emergencies admitted to the hospital to three members of the visiting staff. To the writer was given the supervision of all cases of antepartum haemorrhage and this paper is a review of the cases of placenta praevia seen during the years 1937 to 1944. Twenty-three cases seen in private consultant practice either as "booked" or "emergency" cases are also included. While the writer has not personally delivered all the cases admitted to hospital their treatment has been carried out under his direction.

Antepartum haemorrhage ranks 4th as a cause of maternal mortality in England and Wales and there are 2 large series of cases of placenta praevia collected by Prof. F. J. Browne¹ and Comyns Berkeley² which show the gravity of the condition.

In Browne's series of 3,103 cases the maternal mortality was 5.9 per cent and the foetal mortality 54 per cent. In Berkeley's series of 4,580 cases the figures were 7 per cent and 59 per cent respectively.

In the Royal Maternity Hospital during the years 1932 to 1936, prior to the change of policy described in my opening para-

graph, there were 76 cases admitted, with a maternal mortality of 2.6 per cent and a foetal mortality of 51.3 per cent.

In the treatment of my own series 2 main objectives were:—

(1) The reduction of foetal mortality without unfavourably affecting the maternal death-rate.

(2) The preservation of an open mind with regard to the appropriate treatment of a particular case, i.e., that each case should be treated, not necessarily on any "standard" lines, but in accordance with the conditions found.

The latter objective was in contradistinction to that of Stratz³ who has published a series of 173 cases treated entirely by vaginal methods (rupture of the membranes and bipolar version).

The series referred to, including my own, are summarized in Table I.

I would stress the point that these results are not due to the efforts of any one person but to co-operation by many.

In any case of placenta praevia the attendant who sees the patient first has a great responsibility. He must recognize that, unless in the exceptional event of a serious haemorrhage, the patient should be removed to an institution *without a vaginal*

TABLE I.

| | |
|--|---------------|
| F. J. BROWNE | 3,103 Cases |
| Figures collected from 11 teaching hospitals in Great Britain. | |
| Maternal mortality | 5.9 per cent |
| Foetal mortality | 54 per cent |
| COMYNS BERKELEY | 4,580 Cases |
| Hospitals, Great Britain, Northern Ireland and Eire. | |
| Maternal mortality | 7 per cent |
| Foetal mortality | 59 per cent |
| (S.B. or died) | |
| STRATZ | 173 Cases |
| Maternal mortality | 0.57 per cent |
| Foetal mortality | 44 per cent |
| ROYAL MATERNITY HOSPITAL, 1932-36 | 76 Cases |
| Maternal mortality | 2.6 per cent |
| Foetal mortality | 51.3 per cent |
| (S.B. or died) | |
| ROYAL MATERNITY HOSPITAL, 1937-44 | 174 Cases |
| (Including 23 private cases.) | |
| Maternal mortality | 0.57 per cent |
| (1 case) | |
| Gross foetal mortality | 23.5 per cent |
| (41 cases) | |
| (S.B. or died) | |

examination being made. In this series it is most encouraging to find that in only a few cases had a vaginal examination been made before admission. On admission the

(2) The age, parity and previous obstetric history, with special reference to the size of the babies and the rapidity of labour.

(3) The maturity of the foetus.

(4) The condition of the foetus on admission.

(5) The presence of other obstetric or medical complications.

(6) The type of placenta praevia (only determined when it has been decided that treatment is necessary).

One must decide immediately "Is a vaginal examination necessary?" This decision should be made by someone with experience and not by a resident medical officer. If any real improvement is to be attained co-operation between senior and junior attendants must be enforced at this stage. It is evident from Table II that the number of stillbirths gradually diminished as this policy was increasingly pursued.

It will be noticed that of the 40 deaths which occurred among the babies delivered in the hospital group, 17, i.e. 42 per cent, occurred in the first 2 years. It was during these 2 years that the co-operation between the then senior resident and myself was least satisfactory, many of the cases being examined before I was notified of their admission. The improvement in the later years is largely due to the assistance and co-operation I have received from

TABLE II.
Number of Stillbirths in each Year.

| | 1937 | 1938 | 1939 | 1940 | 1941 | 1942 | 1943 | 1944 | Private |
|------------|------|------|------|------|------|------|------|------|---------|
| | 10 | 7 | 7 | 6 | 0 | 4 | 3 | 3 | 1 |
| Percentage | 58 | 43 | 31.8 | 29.4 | 0 | 17 | 11.5 | 16.6 | 4.3 |

patient's blood should be typed and suitable blood made available in case of necessity. Several factors must be considered before deciding on any line of treatment.

These are as follows:

(1) The amount of haemorrhage.

Capt. Gavin Boyd, Capt. G. A. Craig and Dr. R. A. E. Magee.

There is considerable difference of opinion among authorities regarding the advisability of any vaginal examination in cases of placenta praevia. De Lee⁴ states

"Under a good light the vagina is spread with broad specula and the cervix is inspected for erosions, varices, polyps and cancer. *The fingers are passed into the cervix to feel the placenta.*" (The italics are mine.) Munro Kerr⁵ advises passing a blunt Hegar's dilator through the cervix and moving it about gently; if bleeding occurs the placenta is praevia. Marshall⁶ on the other hand states "I therefore now omit vaginal examination in nearly all those patients whom I intend to deliver by Caesarean section." He further states that the only conditions likely to be missed are carcinoma of the cervix, cervical polyp and ruptured vaginal varix. Can a Caesarean section for a cervical polyp or ruptured varix really be justified?

A vaginal examination should be made in all cases of suspected placenta praevia, but the time at which this examination is made must be carefully chosen.

In the later years of the period under review the attitude adopted has been that *placenta praevia is not an obstetrical emergency which must necessarily be dealt with at the first haemorrhage*, and that a vaginal examination must not be made until the appropriate subsequent treatment can be carried out. There is no objection to passing a speculum and inspecting the cervix but this should be done with great gentleness.

A vaginal examination has been made in every case in this series to determine the type of placenta praevia with which one is dealing and the best method of treatment to employ. It is very easy, but quite unjustifiable, to perform a Caesarean section on every case of placenta praevia without considering all the factors in each case. Many cases are better treated by the vaginal route but it is only on making a vaginal examination that the correct method of treatment can be determined.

One of the main causes of foetal mortality

in placenta praevia is prematurity. This mortality can be reduced only by carrying on the pregnancy to as near term as possible. Several patients in this series have remained in hospital for weeks (1 for 14 weeks) and have had up to 9 haemorrhages before any vaginal examination or manipulative treatment was carried out.

The following arguments can be advanced in favour of this attitude:

(1) The rarity of severe initial haemorrhage in cases of placenta praevia. In my experience this complication rarely occurs apart from vaginal manipulation. Admittedly this is a strong argument in favour of eliminating vaginal examination but if the examination is postponed until as near full time as possible and is not made until the patient is on the operating table with everything at hand to proceed if necessary with an immediate Caesarean section the risk is small.

Severe haemorrhage occurred in 3 cases in this series during the vaginal examination, and in 1 just before an arranged Caesarean was to take place. In only 1 of these cases was a blood transfusion necessary and all the mothers and babies survived.

A sudden severe haemorrhage apart from vaginal examination is theoretically possible in a multipara but is rare in primigravida. The number of primigravidae with Type IV placenta praevia, whose pregnancies have proceeded to term before any haemorrhage occurred, is striking.

(2) A certain number of cases have a sharp but not severe initial haemorrhage at 30 to 34 weeks without any further loss. Some weeks later in some of these cases the placenta can be palpated inside the os without provoking any further bleeding. This has been found to be due to infarction of the separated area. In the cases of this type which have been seen the risk of

further haemorrhage seems to be small even in multiparae. Figure 1 illustrates the findings in such a case.

(3) There are a large number of cases of antepartum haemorrhage with a history apparently typical of placenta praevia when the haemorrhage is either not due to a low-lying placenta or due to a degree of placenta praevia which can be safely treated by methods other than Caesarean section. I cannot agree with Marshall's statement that "the history alone enables the junior house surgeon in his first few months of residence to diagnose the condition with almost 100 per cent accuracy." To give but one example of many such cases:

Mrs. C., aged 31, 5th pregnancy. Admitted to the antenatal ward at 35 weeks on account of severe anaemia. The haemoglobin was 25 per cent. She received the usual treatment for such a case including a blood transfusion. While lying in the ward she had a sudden painless haemorrhage at term, losing about 1 pint of blood. She was taken to the theatre with the intention of doing a Caesarean section without delay and without a preliminary vaginal examination.

At the last moment this decision was reconsidered and on vaginal examination the placenta could not be felt. The membranes were ruptured and the baby was delivered spontaneously 2 hours later. The baby was alive and on examination of the placenta and membranes the opening in the membranes was as far away from the edge of the placenta as it could possibly be.

In this series, 81 cases, or 47.6 per cent, were treated at the time of the initial haemorrhage. In the earlier years it was difficult to rid one's mind of Jaggard's dictum "there is no expectant plan of treatment for placenta praevia" but with increasing experience the proportion of those patients who were treated immediately following the first haemorrhage gradually diminished.

From the experience gained over the last 8 years one feels that there is a very

definite place for expectant treatment, even after the patient has had several small haemorrhages.

Among these patients there has been nothing to confirm the belief that the recurrent haemorrhages tend to lead up to a catastrophic haemorrhage. Many patients have been under observation for weeks during which numerous small haemorrhages have occurred without causing any serious anxiety. Naturally, if a haemorrhage should occur while the patient is under observation and approaching term, e.g. 38 weeks, treatment is carried out at that stage to avoid the risk of further loss of blood. This attitude has meant that the infant's chance of survival is much enhanced. The additional complication of prematurity is lessened or may even be eliminated. This is borne out by the figures of Table II and also by comparing the weights of babies in the early years of the series with a similar number delivered more recently. In the last 47 cases the average weight of the babies was 6 pounds 12 ounces while the average of the first 47 cases in the series was only 5 pounds 2 ounces. In addition the foetal mortality in the 47 early cases was 47 per cent, whereas in the last 47 cases it was only 6 per cent.

TABLE III.

| | Average weight | | Mortality |
|----------------|----------------|-----------|-------------|
| First 47 cases | 5 pounds | 2 ounces | 47 per cent |
| Last 47 cases | 6 pounds | 12 ounces | 6 per cent |

I do know that in the early cases one was alarmed by and treated haemorrhages which, with experience, one would now definitely leave without interference. If one is to judge by these figures there is a very strong argument in favour of expectant treatment, as far as the baby is concerned, and, as the maternal mortality has

not risen, the result appears to be quite justified.

In this series there were 33 primigravidae, representing 18.8 per cent of the total series. Of these only 4 patients were under 36 weeks gestation at the time of delivery. Of the 33 patients 4 had had more than 1 warning haemorrhage and 10 had had one warning haemorrhage. There were 19 cases in which the patient was either admitted and treated for the initial haemorrhage or where the presence of a placenta praevia was unsuspected, the patient having been admitted for the treatment of other complications. Of these 19 cases only 3 patients were under 38 weeks gestation.

Particular mention of 6 primigravidae must be made. In 5 of these no haemorrhage of any kind occurred during pregnancy. The presence of the placenta praevia was not discovered until examination or treatment was instituted for the obstetric complication which had necessitated the patient's admission.

One was a diabetic upon whom a deliberate Caesarean section was being performed at 36 weeks when the placenta was found to occupy a large part of the lower uterine segment. Another case was referred to me on account of a head free above the pelvic brim at 36 weeks. On X-ray examination the foetus appeared to be normal but there was marked extension of the head and neck. When this patient had passed the calculated date the foetal heart-rate increased to an alarming degree, so a Caesarean section was performed. The placenta was covering the internal os and filling the lower uterine segment at operation. This patient had no uterine loss for 3 days following operation during which time she developed a reflex ileus. A cervical dilatation had to be done before the uterus would drain. This unexpected complication (? stenosed os) may have

accounted for the absence of any antepartum haemorrhage.

The 3rd case was a primigravida of 33 years, admitted to hospital on account of disproportion. At operation the head was floating above the brim and on incising the lower uterine segment the placenta was divided. The position of the placenta was almost certainly the cause of the apparent disproportion.

The 4th case was admitted on account of pre-eclamptic toxæmia and a free head at 39 weeks. Eleven days after admission the patient was examined vaginally and the cervix was found to be partially effaced and, on passing the finger into the canal, the placenta was felt and a profuse haemorrhage occurred.

The 2 remaining cases were both suffering from pre-eclamptic toxæmia and were admitted to hospital for induction of labour. Prior to the induction one had a small haemorrhage, which was regarded as being accidental in type, but on passing a bougie severe haemorrhage occurred after which the placenta could be felt. The other case was being examined prior to inserting a bougie when the internal os was found to be covered by placenta. I have had a similar experience with a 2-para whom I was inducing for pre-eclamptic toxæmia at term. In this patient there was no history of antepartum haemorrhage, the first haemorrhage occurring when I separated a small area of the placenta which was covering the internal os.

These cases illustrate what is not generally recognized, namely that a placenta can be praevia without causing any haemorrhage until the cervix begins to dilate or until some vaginal manipulation is carried out.

Three primigravidae had a marked intrapartum loss and in these cases the placenta was not felt until the cervix would admit 2 fingers. In one of these cases the head

that the foetus was anencephalic. Foetal heart sounds could not be heard.

At 2 a.m. on the following day the patient delivered herself of a stillborn anencephalic foetus; this was followed 10 minutes later by the placenta and membranes.

The foetus was not macerated; it was of about 28 weeks maturity and anencephaly was the only deformity. It weighed 1 pound 2 ounces and measured 14 inches in length. There was a direct communication between the meninges and the exterior. The alimentary canal was patent throughout its length. The stomach contained about 2 c.cm. of fluid; this was not analysed. The kidneys and bladder were normal in appearance, the uterus and urethra were patent and all other organs were normally developed. The placenta weighed 5 ounces, its macroscopic appearance was normal and there was no evidence of old or recent infarcts. Microscopic section did not show any abnormality. The cord measured 9 inches in length and there were no twists or knots to suggest obstruction. The chorion and amnion were normal in macroscopic appearance. Microscopically, the epithelium of the amnion appeared less tall, more deeply stained, and less vacuolated than in the controls. The amniotic fluid was of normal appearance; unfortunately the specimen for analysis was contaminated and rendered useless.

DISCUSSION.

Many of the cases reported as acute hydramnios cannot in fact be so regarded (if we limit the term to cases which occur within the space of a few days), though possibly they might be regarded as sub-acute. The majority of cases occur in association with some type of foetal deformity or maternal disease, which is also usually found in the chronic variety. A study of these cases also reveals the fact that in none was there very rapid accumulation of massive quantities of fluid; it was in fact the symptoms that were of sudden origin. These symptoms were not purely mechanical in origin, due to pressure, but were those of over-distention of a hollow organ, namely, pain and reflex vomiting.

Gaechtgens,¹⁰ reporting 2 cases of acute hydramnios, both associated with uniovular twins, noted that one of the patients had received a blow on the abdomen 24 hours before the onset of symptoms, and is of opinion that this trauma was a stimulus. In the case here reported, a very careful study of the history for some weeks prior to the onset of the acute hydramnios failed to reveal any evidence of trauma, either physical or mental, and the habits and diet of the patient had not changed in any way. A striking feature, however, was the extreme spasm of the abdominal and uterine musculature. Possibly the uterine musculature of this patient was more sensitive than usual to undue stretching, and an accumulation of fluid which would ordinarily have been accommodated without much difficulty caused the muscles to go into spasm and produce the alarming symptoms. In twin pregnancy, the available uterine space is already very much encroached upon and the uterine musculature is over-stretched, so that a very little extra accumulation of liquor will be more serious.

The normal power of expansion of the uterine musculature is very remarkable, and upwards of 10 pints of fluid can often be quite readily accommodated without symptoms, except those of mechanical origin.

In this case pathological examination, both macroscopic and microscopic, of the amniotic epithelium did not reveal any evidence of acute inflammation or of any undue secretory activity. Examination of the placenta, liquor amnii and blood of the mother for syphilis and for Rh-agglutinins also proved negative. The amount of liquor was excessive, but not enough to produce pressure symptoms and not so great that it could not have been easily accommodated in the ordinary way. All the symptoms and physical signs were those

of over-stretching of the uterine musculature.

We may conclude that acute hydramnios apparently occurs in patients who would, in any case, develop hydramnios slowly, but owing to the introduction of an additional factor, namely muscle which is over-sensitive to undue stretching, especially in the presence of an extra amniotic sac, and sometimes following trauma, symptoms arise acutely.

SYMPTOMS AND SIGNS.

The symptoms of distension of a hollow organ will predominate rather than those of pressure; the latter will develop subsequently. Pain is the most outstanding feature. In the very early stages, the patient usually complains of an uncomfortable sensation of tightening across the abdomen; this very rapidly gives place to a very severe abdominal pain, radiating over the whole abdomen, over the sacrum, and often down the thighs. Vomiting becomes severe and persistent, often producing thirst for loss of fluid.

In the true acute variety, the signs are not those of great accumulation of fluid, but rather those of abdominal and uterine muscle spasm. The abdomen is tense, tender, and difficult to palpate; foetal parts are usually impossible to feel owing to muscle spasm, abdominal tenderness and, to a lesser degree, presence of excess liquor. The foetal heart sounds are often not heard. The degree of abdominal enlargement and the presence of ballottement will depend upon the amount of fluid, and in the true acute type these are not prominent features. The pulse-rate increases and the temperature may be raised, though usually it is not. Albuminuria is not a constant feature, and when present its quantity has no relation to the amount of hydramnios. In this case, and also in that described by Calatozzolo,²² the blood-

pressure was raised, but in the others it does not appear to have been affected. If treatment be not instituted the abdomen enlarges, signs and symptoms of pressure become more obvious, with dyspnoea, pain under the diaphragm, and oedema of the legs. Vaginal examination will reveal the usual signs of pregnancy, and if the cervix admits the tip of the finger a point of peculiar diagnostic significance will be the tense, bulging membranes.

DIFFERENTIAL DIAGNOSIS.

Concealed accidental haemorrhage.

Although in many textbooks this condition is not mentioned in discussing differential diagnosis, if we study the reported cases it would seem to assume first place. Calatozzolo,²² in his case of acute hydramnios made an erroneous diagnosis of premature separation of the normally situated placenta.

Courtois²³ reported a case diagnosed as acute hydramnios which later proved to be one of concealed accidental haemorrhage. The case here described presented many features strongly suggesting concealed accidental haemorrhage—rapidity of onset of pain, vomiting and poor general condition, a tender, woody abdomen, loss of sensation of foetal movements and absence of the foetal heart sounds. The symptoms and signs are all the more misleading if there should be little abdominal enlargement and a rise of blood-pressure.

The main points of difference are: (i) the duration of symptoms—in acute hydramnios the patient, on close questioning, will often admit having had abdominal discomfort for many hours prior to the onset of acute pain; (ii) the abdominal enlargement is often, though not always, great enough to make the possibility of internal haemorrhage unlikely; (iii) ballottement, if elicited, will favour a diagnosis of hydramnios; (iv) investigation of the previous history

may help; (v) occasionally even these differential signs are absent and it is in such cases, when the diagnosis is still in doubt, that Courtois²³ recommends abdominal puncture of the uterus by a fine needle. This procedure will be required to lower the intrauterine pressure, so that nothing is lost by it. If blood-stained liquor is recovered, the subsequent treatment will be that of haemamnios. On this finding Courtois revised his original diagnosis and altered his treatment accordingly. X-ray examination will, of course, help, and should always be carried out in these cases, the presence of a foetal deformity favouring hydramnios. In the early stages of gestation it may be necessary first to establish the existence of a pregnancy. This difficulty was not met with in any of the cases described since 1914.

Other conditions mentioned in the textbooks as requiring differentiation are, occasionally, ovarian cyst, ascites and multiple pregnancy. In all the cases reviewed, the only condition which required differentiation was concealed accidental haemorrhage.

TREATMENT.

If the foetus is normal, an effort is made to carry the pregnancy to term. This can occasionally be achieved by frequent decompression of the uterus through the abdomen. If the foetus is deformed or the pregnancy is at term, labour may be induced forthwith. The best method is by gradually draining off the liquor by a fine needle through the abdominal wall; by this means the membranes remain intact and labour comes on slowly. The next best method is by rupture of the hindwaters with a Drew-Smythe catheter.

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Treatment with Penicillin of Some Obstetric Cases

BY

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THE following account of the use of penicillin presents illustrations of its value in cases of sepsis in obstetrics. The patients, who were all treated at the County Infirmary, Carmarthen, consisted of 5 cases of Group A haemolytic streptococcal infections of the genital tract with complications, and 2 cases of bullous impetigo in neonates.

The 5 cases of streptococcal infection were first treated with sulphanilamide. The routine dosage employed was 2 g. initially, a further 2 g. in 4 hours and then 1 g. 4-hourly. This treatment was started as soon as there was rise of temperature or pulse-rate. Bacteriological examination was immediately carried out on vaginal, nose and throat swabs, and a catheter specimen of urine. Penicillin treatment was started only when it became clear that the infection was not being controlled by sulphanilamide.

CASE I.

Mrs. A. D., aged 35, a 5-gravida, had nothing relevant in her previous obstetric history. She was admitted at term as an emergency on September 12th, 1944, in the first stage of labour. There was a history that the patient had been in bed at home for a fortnight before admission with pyrexia and a left facial palsy. On admission to an isolation ward her temperature was 102.6°F. and her pulse-rate 120 per minute. Her general condition was poor; there was a left facial palsy and a dry, fibrosed perforation of the left tympanum. Other abnormal physical signs were not found. Her labour was uneventful and she was delivered naturally of a healthy infant an hour later. Sulphanilamide therapy was started immediately and bacteriological investigations were carried out. The

temperature settled the morning after delivery but the pulse-rate remained at 100 per minute. The bacteriological examination showed a heavy growth of Group A haemolytic streptococci in the vagina alone (the ear swab being among the negative findings). On September 14th (2nd day of puerperium) the patient's abdomen became distended and she developed generalized abdominal tenderness. Her general condition deteriorated. A provisional diagnosis of general streptococcal peritonitis was made, and the abdomen was opened the same day through a small low median incision. There was some serous exudate and the small bowel was distended. The exudate was aspirated and on direct culture grew Group A haemolytic streptococci. A tube drain was left in the abdominal wound for 3 days. On September 15th, as there was still further deterioration in the patient's general condition, penicillin therapy (15,000 units 3-hourly) was started and the sulphanilamide discontinued. The pulse-rate began to settle the day after penicillin was started. It was given for 4 days and then stopped. The haemoglobin level on September 18th was 52 per cent and the patient was given a transfusion of 2 pints of fresh blood.

There was a further rise of temperature and pulse-rate on September 22nd, and again on September 25th, when penicillin (15,000 units 3-hourly) was restarted for another 4 days. The temperature and pulse-rate again settled—this time in 3 days. At this stage the patient became fractious and was difficult to manage. She objected strongly to the pain of the penicillin injections and discharged herself against advice on October 2nd, the 20th day of the puerperium. Her general condition was then fairly good, the abdominal wound was healed and the facial palsy improved.

She was readmitted a fortnight later (on October 17th) with a history of intense headaches, vomiting, drowsiness and pyrexia for the previous

week. She was now running a remittent pyrexia. There was bilateral papilloedema with a patchy retinitis and a left facial weakness. The abdomen did not show any abnormality. The cervix was healthy, the uterus well involuted and the appendages normal. Routine bacteriological examination did not show haemolytic streptococci in the vaginal swab. Lumbar puncture revealed a normal cerebrospinal fluid. She was transferred to Oxford under the care of Mr. J. Pennybacker as a possible cerebral abscess. Investigations at Oxford showed that she had a cerebral thrombophlebitis. From October 26th to November 8th she had a further 1,900,000 units of penicillin at Oxford. She returned to Carmarthen on November 18th and went home on the 21st in good health.

Comment. There is considerable evidence that the sulphonamides have reduced the incidence of general peritonitis as a complication of streptococcal infections of the genital tract. Streptococcal peritonitis still has a high mortality even with sulphonamide therapy. It remains to be seen whether or not the use of penicillin—as illustrated above—will be a more effective form of treatment. In this particular case the initial course of penicillin was undoubtedly too short (penicillin at the time was difficult to get for civilian use).

CASE 2.

Mrs. H. M. L., a primigravida aged 26, was admitted on September 12th, 1944. She was a florid, obese patient who had hypertensive toxæmia throughout her pregnancy. She was admitted at the 38th week because of the sudden appearance of oedema and albuminuria in addition to the long-standing hypertension. In view of this and of the fact that her sister had had postnatal eclampsia 2 years previously, labour was induced by sweeping and rupturing the membranes after premedication. She had a spontaneous delivery of a live infant. An hour later she had an eclamptic fit and was given 500 c.cm. of 40 per cent glucose intravenously and morphia gr. $\frac{1}{2}$. She had 7 more eclamptic fits within 12 hours, was given more morphia and intravenous glucose and 1 pint of

blood was withdrawn by venesection. She eventually settled down 15 hours after delivery.

On September 16th (4th day of the puerperium) she developed a temperature of 99.5°F. with a pulse-rate of 136 per minute and was isolated. Sulphanilamide was started. The vaginal swab showed a very heavy growth of Group A haemolytic streptococci. On the 7th day of the puerperium her temperature rose to 103°F. with a pulse-rate of 120 per minute. She developed abdominal distension and generalized abdominal tenderness. The abdomen was drained the same day through a small lower median incision. Fluid taken from the abdomen at operation did not grow any organisms, but fluid taken from the drainage tube 3 days later grew haemolytic streptococci.

The temperature began to show signs of settling, but rose again to 101°F. on September 26, and a vaginal swab on that day still showed a very heavy growth of Group A haemolytic streptococci. Sulphanilamide therapy was continued and repeated white-cell counts were done. On October 7th, after 21 days of sulphanilamide, came the first warning of agranulocytosis. The white cell count on that day was 4,550 per c.mm. with 30 per cent polymorphs and 51 per cent lymphocytes. The sulphanilamide was discontinued and Pentnucleotide (40 c.cm. daily and Vitamin C (600 mgm. daily) were given. Daily white cell counts showed gradual deterioration and on October 10th the total white cell count was 3,400 per c.cm. with only 4 per cent polymorph neutrophils and 1 per cent basophils.

In view of the facts that the patient still had a heavy streptococcal infection, that she was deprived of her natural cellular defences and that further treatment with sulphanilamide was dangerous, penicillin therapy was started on October 10th. The patient was given 15,000 units 3-hourly and this was continued until the white cell count returned to normal on October 17th, by which time the temperature and pulse-rate had also settled. Between October 10th and 17th the patient was also given alternate daily transfusions of 1 pint of fresh blood, daily parenteral liver ("Examen" 4 c.cm.), in addition to the Pentnucleotide and Vitamin C.

After October 17th the patient made steady progress. She had developed a superficial thrombophlebitis in the left leg on October 15th, which

gradually subsided. She was discharged in good health on November 10th. Postnatal examination on December 14th revealed a blood-pressure of 145/80, and a healthy pelvis.

Comment. In this case the general peritonitis had subsided before penicillin was started. It was the onset of a severe agranulocytosis with the heavy streptococcal infection persisting in the genital tract that provided the indication for penicillin. Superficial thrombophlebitis is a not uncommon complication of penicillin therapy.¹

CASE 3.

Mrs. W.B., a primigravida aged 32, was admitted on October 30th, 1944, and had a normal delivery of a full time infant. On the 3rd evening of the puerperium she developed a temperature of 103.6°F. and a pulse-rate of 120 per minute. She was isolated and given sulphanilamide therapy. Routine bacteriological examination showed a very heavy growth of Group A haemolytic streptococci in the vagina. The temperature and pulse settled gradually, but on the 10th day of the puerperium both rose again (temperature 101°F. to 102°F.; pulse 120 a minute). The temperature and pulse settled again in another 4 days, and on the 17th day the sulphanilamide was discontinued.

On the 24th day of the puerperium there was another sharp rise of temperature to 104.6°F. and of the pulse-rate to 136 per minute. The vaginal swab on that day still showed a heavy growth of haemolytic streptococci and sulphanilamide treatment was restarted. On the 25th day of the puerperium the white cell count was 6,000 per c.cm. with only 39 per cent polymorphs. Sulphanilamide was discontinued and penicillin (15,000 units 3-hourly) was given together with Pentnucleotide, 40 c.cm. daily. The Pentnucleotide was stopped after 3 days and the penicillin after 5 days. The pyrexia and rapid pulse-rate settled the day after penicillin therapy was begun. The clinical appearance of the patient improved rapidly and she was discharged in good health on December 5th; the 37th day of the puerperium. Postnatal examinations on December 23rd showed a healthy cervix, a uterus well involuted, and normal appendages.

Comment. The indication for penicillin in this case was similar to that in Case 2. The only difference was the degree of agranulocytosis.

CASE 4.

Mrs. E. A. J., aged 33, a 6-gravida, was admitted in labour on March 23rd, 1945, as a case of pre-eclamptic toxæmia. She was at term, her blood-pressure was 170/90, the urine was loaded with albumin and there was oedema of the legs. She had a spontaneous delivery. On the 3rd day of the puerperium she complained of a sore throat, had a temperature of 101.5°F. and a pulse-rate of 110 per minute. She was isolated and given sulphanilamide. Routine bacteriological investigations showed a very heavy growth of Group A streptococci in the vagina alone. On the 3rd day of treatment the haemoglobin was 50 per cent and the patient was transfused with 1 pint of fresh blood. There was no improvement after 6 days and penicillin was started. Both temperature and pulse settled on the following day. Penicillin was continued for another 5 days. On April 7th, 2 days after it was stopped, the temperature and pulse rose again. The left leg became oedematous and painful and there developed a clear picture of femoral thrombophlebitis. Bacteriological examination on April 7th did not show any haemolytic streptococci in the vaginal swab. Further penicillin was not given. The haemoglobin level was still only 64 per cent on April 8th, and a further transfusion of 1 pint of concentrated red cells was given. The thrombophlebitis subsided without incident, and the patient was discharged in good health on May 25th. Postnatal examination on that day showed an old laceration of the cervix, a well involuted uterus, and normal appendages.

Comment. Clinical response to sulphonamide therapy was not evident after 6 days, and on this indication penicillin was started with striking effect.

CASE 5.

Mrs. F.O., aged 23, a primigravida, was admitted on September 28th, 1944, at the 39th week of a twin pregnancy for pre-eclamptic toxæmia. Labour was induced by sweeping and rupturing the mem-

branes and live infants were delivered without incident. On the 4th day of the puerperium she developed a temperature of 103°F. and a pulse-rate of 130 per minute. She was isolated and given sulphanilamide. Routine bacteriological examination showed a very heavy growth of Group A haemolytic streptococci in the vagina. She ran an intermittent pyrexia which settled on the 12th day of the puerperium and she discharged herself against advice on the 13th day (October 14th).

She remained at home in indifferent health and 3 weeks later she became acutely ill and was readmitted to hospital on November 7th. On admission she had a temperature of 104.8°F. and a pulse-rate of 128 per minute. She complained of a great deal of pelvic pain. She had a large, tender, fixed mass in the right side of the pelvis and the uterus was pushed over to the left. Penicillin (15,000 units 3-hourly) was started at once. The temperature was normal the next day but the pulse-rate was still high—118 per minute. The same day (November 8th) the pouch of Douglas was explored by a posterior colpotomy. Pus was not found and a small de Pezzer tube drain was left in the incision for 3 days. The fluid from the tube was sterile and the vaginal swab grew coliform bacilli only. The pulse-rate gradually settled and the temperature did not rise again. The pelvic mass gradually resolved, and during its resolution it became more and more obvious that it was a parametritis. Penicillin was stopped after 7 days. A striking feature of this case was the marked improvement in the clinical condition of the patient effected by penicillin in 1 week. She was discharged on November 27th in good health. Postnatal examination on December 16th revealed a healthy cervix, the colpotomy wound healed, and the uterus, parametrium and appendages all normal.

Comment. The swift response to penicillin suggests that the parametritis, which followed a streptococcal genital tract infection, was due to a penicillin-sensitive organism. The swabs from the de Pezzer tube drain and the vagina were taken 20 hours after penicillin was started. It is possible that the negative swab findings may have resulted from this amount of penicillin therapy.

CASE 7.

Infant B. was born on July 23rd, 1944. The delivery was at term and was normal. On July 27th the baby developed bullous impetigo—first in the folds of the neck and eventually over most of the body. Swabs showed a very heavy growth of *Staphylococcus aureus*. At the time there was an outbreak of bullous impetigo in the nursery. The affected infants were isolated and their lesions and cord stumps were dusted with sulphathiazole powder. The ruptured bullae were dried before the powder was applied. Most of the infants responded to this treatment. In the case of Infant B the lesions kept on spreading and red indurated areas developed round some of them. Penicillin ointment was applied after 8 days of sulphathiazole powder and the condition began to subside. The ointment was applied 8-hourly, and the lesions were cleared in 6 days. The infant's general condition was much improved.

CASE 8.

Infant J., born on July 29th, 1944, was a similar case. Penicillin ointment was applied to the lesions after 3 days initial trial with sulphathiazole powder. The rash cleared in 7 days.

Comment. Staphylococcal bullous impetigo has been a troublesome infection in nurseries in the last few years. Its control has been thoroughly investigated recently. Penicillin ointment, properly prepared and handled, offers a simple therapeutic measure well worthy of further trial.

CONCLUSIONS.

In the cases described the patients were very ill. The first 2 patients, in spite of early sulphonamide-treatment, developed peritonitis. In Cases 2 and 3 sulphonamides were pushed to the stage at which agranulocytosis developed—a complication as dangerous as the original infection. Before penicillin was available there was no further line of treatment, and it is probable that Case 1, and possible that Cases 2 and 3, would have died. The rapid

improvement with penicillin was therefore all the more striking.

The cases are few in number and it will be some time yet before the value of penicillin can be fully assessed and compared with that of the sulphonamides.

My thanks are due to Drs. R. M. Fry and J. M. Boissard of the Emergency Public Health Laboratory, Carmarthen, for the bacteriological work and for their

active interest and guidance, and to Professor Miles H. Phillips for his clinical help and advice.

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A Case of Meigs's Syndrome

BY

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LAWSON Tait¹ described a condition in women in which he found both ascites and hydrothorax. He did not think that these findings were always pathognomonic of cancer and even at that time advised laparotomy in such cases. The presence of ascites, hydrothorax and an ovarian fibroma is well established as a syndrome bearing the name of Meigs² since he and his colleagues first recognized this triple condition. Gardiner and Lloyd-Hart³ estimated the number of reported cases as 38, including 1 of their own. Since this publication, Clay *et al*⁴ in Britain have published 2 more. Kehidai⁵ in Hungary has added another and with the case described below the total is now 42. By far the majority of cases have been reported from America.

CASE REPORT

H.K., 26 years old, resident in Istanbul, 9 years married, 1 child 7 years old, was admitted to 2nd University Obstetric Clinic on May 31st, 1943. She complained of abdominal swelling and breathlessness which had started 9 months before. In the previous winter she had been treated for pleurisy. Menstruation had always been regular.

Clinical examination. The patient, of average build, had cyanosis of the face and dyspnoea. The heart was shifted to the left but the sounds were normal, pulse 108, blood-pressure 135/90. There was a right pleural effusion. The abdomen was distended with fluid and in the hypogastrium was a hard and irregular tumour, the size of a foetal head. On vaginal examination the uterus could be felt normal in size but lying behind the tumour. Urine was normal. *Blood:* Haemoglobin 86 per

cent (Sahli), erythrocytes 5,000,000; leucocytes 10,400 (differential count—eosinophils 1 per cent, polymorphs 74 per cent, band forms 2 per cent, lymphocytes 20 per cent, monocytes 3 per cent). Sedimentation rate (Westergren) $\frac{1}{2}$ hour, 8 mm.; 1 hour, 52 mm.; 2 hours, 90 mm.

Diagnosis. A solid tumour of the ovary with ascites—fibroma or carcinoma. In view of the pleural effusion, consultation with a physician was arranged. The pleural effusion was considered to be an aftermath of the attack of pleurisy during the previous winter.

Treatment. Conservative treatment was advised by the medical specialist—low salt diet, calcium, vitamin C, cardiac tonics. Fig. 1 is a radiogram of the chest taken on June 5th, 1943. On June 21st 1,200 c.cm. were aspirated from the pleural cavity. The fluid was serofibrinous, dark yellow, Rivalta positive, density 1.015, albumin 6 g. per litre, erythrocytes and leucocytes were present. Fluid was found at the same level in the pleural cavity (Fig. 2) the day after the aspiration and dyspnoea had returned. On July 5th a second aspiration (2,000 c.cm.) was performed. Two days later a further radiogram was taken and the fluid was found at the old level. In view of the persistence of the effusion, the marked dyspnoea and the orthopnoea it was decided to do a laparotomy.

Laparotomy (July 19th, 1943). Just before the operation 2,750 c.cm. of fluid were aspirated from the pleural cavity. Spinal anaesthesia (5 c.cm. of 2.5 per cent novocain solution) was used. An ovarian tumour was removed and also 2 litres of blood-stained fluid.

Pathological anatomy. The tumour was solid with a thin capsule, the cut surface showed whorls of fibrous tissue. Cystic spaces were absent. Histologically there was no lipoid and no epithelium but the tissue was rich in cells. *Diagnosis—fibroma of ovary.*



FIG 1
Before aspiration



FIG 2
One day after aspiration

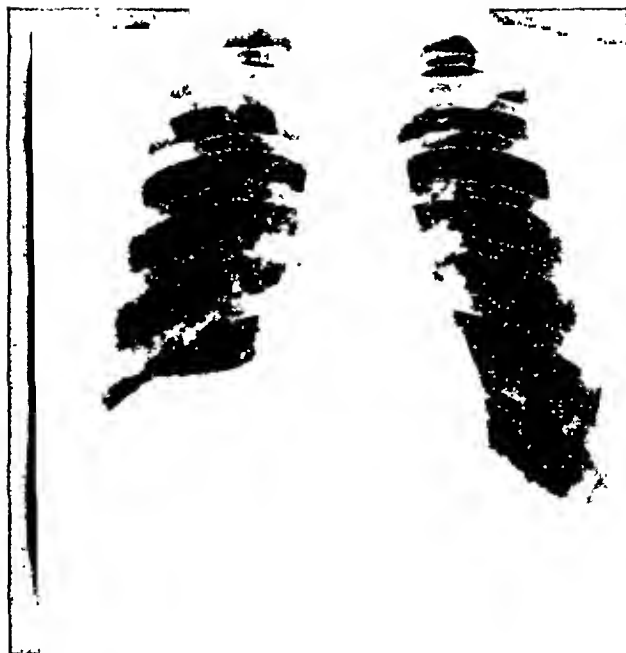


FIG. 3.
Fifteen days after removal of tumour.
Dome of diaphragm raised.



FIG. 4.
Eight months after operation. Diaphragm normal.

Post-operative course. Dyspnoea disappeared very rapidly. Convalescence was uninterrupted and the patient was out of bed on the 9th day. On August 3rd, 15 days after the operation, radiography (Fig. 3) showed complete disappearance of the pleural effusion but the dome of the diaphragm was raised. The patient was seen several times later and radiographs taken. The last of these (Fig. 4) was on March 1st, 1944—8 months after the operation—and showed the pleural cavity to be free of fluid and the level of the diaphragm normal.

DISCUSSION.

The association of ascites with an ovarian fibroma is well recognized and occurs in about 40 to 75 per cent of cases, but the presence of a pleural effusion as well is rare. There appears to be no relation between the amount of fluid in each cavity.

Several authors have attempted to explain the phenomenon. Meigs and his collaborators⁶ in 2 of their cases injected 20 c.cm. of Indian ink into the abdominal cavity and found the fluid in the chest to have the same concentration of ink as that in the abdomen. There was no evidence that the ink had travelled by the bloodstream. They suggested that the fluid reaches the pleural cavity from the abdomen by way of the diaphragmatic lymphatics. Meigs also introduced air into the pleural cavity but none of it passed into the abdomen. The reverse procedure did not have any positive result.

Gardiner and Lloyd-Hart³ consider that obstruction to the venous return to the heart is the most likely explanation of the hydrothorax. In a clinical review of the published cases they have noted that in 1 autopsy the azygos vein was twice as wide as the abdominal aorta. In some patients

there has been oedema of the feet. Hydrothorax is nearly 4 times more common on the right than on the left side. Sometimes the tumour has been found impacted in the pelvic cavity. With pressure on the lower part of the inferior vena cava, an increased amount of blood must pass along the azygos system. Owing to the inefficiency of the valves in the upper part of the azygos vein back-pressure and also transudate into the pleural cavity may result.

Pleural effusion and ascites may be found in hepatic, renal or cardiac disease, tuberculosis or carcinomatosis. It is probable that cases of Meigs's syndrome are missed and the patient denied the chance of cure by early operation. This disease serves to emphasize the importance of close liaison between the physician and gynaecologist. In all cases of co-existent hydrothorax and ascites in women a pelvic examination is essential.

SUMMARY.

1. A case of Meigs's syndrome is reported which makes the total number so far recorded 42.
2. The theory that the pleural effusion results from back-pressure in the azygos system is supported.

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Carcinoma of the Female Urethra

(Review of the Literature and Report of Three Cases.)

BY

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My interest in carcinoma of the female urethra was stimulated after encountering 2 cases in a year, and a third case that occurred in the same Emergency Medical Service Sector is added. The cases are not of themselves especially noteworthy, although the condition is a rare one, but this review is presented as there has not been any recent account in the British literature. Boivin and Dugès¹ first recorded a case of carcinoma of the female urethra in 1833, and subsequently Menville² collected 149 cases (up to 1935). Many of the reported cases are incompletely described, and in particular histological details are often missing. Another difficulty is that in advanced cases the disease spreads widely, so that it may not be possible to demonstrate its site of origin with certainty; and conversely vulvovaginal growths may invade the urethra.

Urethral carcinoma appears to be commoner in the female than in the male; Nichol³ stated that 149 cases had been reported in males and 262 cases in females. The true incidence of carcinoma of the female urethra is difficult to establish. Hamann and Göbel⁴ found that it accounted for 0.16 per cent of gynaecological carcinoma, but Menville² found only 1 instance among 43,000 gynaecological cases. Sarcoma of the female urethra is still less common, only 22 cases having been reported.

Etiology. Urethral carcinoma is usually a disease of the postmenopausal woman,

the average age in 109 cases being 53 years (Menville²) but it is seen in younger women, as for example Watson's⁵ patient, aged 27.

In the male, urethral carcinoma frequently follows stricture or fistula (Scholl and Braasch⁶), but in the female predisposing factors are less definite. The disease is mostly seen in parous women, and following Ehrendorfer⁷ most authors have mentioned trauma or chronic inflammatory processes as etiological factors. Hallé⁸ claimed that leukoplakic changes could be discovered in the urethra in cases of carcinoma, but I have not found any confirmation of his observations, and, so far as the vulvo-urethral type of growth is concerned, this is an unlikely event, for the vestibule is usually exempt from the changes of leukoplakic vulvitis. Urethral caruncle is sometimes suspected to be a predisposing lesion, but in view of the frequency of occurrence of caruncle, it is hard to be sure that the supposed relation is not merely that of chance. In the second case below, some evidence is brought forward to suggest that malignant change may occasionally occur in a caruncle, though it is not suggested that it is a common event.

I have looked through the notes of 82 cases of caruncle and examined most of the sections, but cannot find other clinical or histological suggestion of any relation between caruncle and carcinoma, though 4 of the caruncles were recurrent.

Pathology. Following Winckel, Whitehouse⁹ divided the cases into urethral and

vulvo-urethral types, and the latter are found about twice as often as the former. Whitehouse's account of the gross pathology is still one of the most valuable, and it is difficult to add much to his description:

A. Urethral carcinoma. This is seen in two common forms: (1) In the usual form the growth appears as a malignant ulcer in the urethral floor, most often in the distal urethra. (2) The less common form is that of periurethral induration, extending for some length along the urethra, and ulceration is late.

B. Vulvo-urethral carcinoma presents in 3 forms: (1) A vascular papillomatous nodule at the posterior margin of the urethral orifice. (2) A nodule that breaks down to an ulcer in the vestibule. (3) A scirrhus induration around the urethral orifice.

On microscopical examination the neoplasms are found to be of varying type, but the lack of exact histological data in many of the reports makes exact statistical statement impossible. Squamous cell carcinoma, columnar cell carcinoma (both simple and adenocarcinoma), mucoid carcinoma, and undifferentiated types all occur. In most series squamous cell carcinoma predominate. The following figures are based on the reports of Menville,² Nichol,³ Watson,⁵ Scholl and Braasch,⁶ Whitehouse,⁹ Palmer,¹⁰ Pugh,¹¹ Pomeroy,¹² Menville and Counsellor,¹³ Sparks and Parsons,¹⁴ Sala and Levine,¹⁵ Tuta and Hess,¹⁶ as these cases are all fully reported, and the present cases are added. Among 27 cases of urethral carcinoma there were 12 cases of squamous cell carcinoma, 10 of columnar cell carcinoma (4 of these were adenocarcinomata), and 5 of undifferentiated carcinoma. Among 42 cases of vulvo-urethral carcinoma there were 31 cases of squamous cell carcinoma, 9 of columnar cell carcinoma, 1 of mucoid carcinoma, and 1 of undifferentiated carcinoma. In the whole

series 64 per cent were squamous cell carcinoma.

Menville² has stressed the similarity of the growths to neoplasms of the bladder. It is also suggested that the well differentiated adenocarcinomata may arise from the paraurethral glands, but this statement is conjectural rather than proven. The squamous cell neoplasms appear to be radiosensitive, but evidence is incomplete about the other types.

Clinical features. Urethral carcinoma does not produce much discomfort in the early stages, and, even after severe symptoms appear, patients so commonly delay seeking advice that extension to bladder, vagina or lymph nodes may have already occurred by the time the patient is seen.

Perhaps the commonest of the early symptoms is painful micturition. In some cases, particularly of the sclerosing type of growth, difficult micturition or retention may occur; in other cases, frequency. Bleeding is a common symptom, more especially with micturition, but, in the case of growths projecting from the urethra, at other times also. Local tenderness and dyspareunia also occur with the more superficial growths. Some of the patients may report a swelling in the region of the urethra, or even in the groin, when inguinal metastasis has occurred. The symptoms naturally vary with the type of neoplasm; the papillomatous vulvo-urethral type chiefly causes haemorrhage and pain, in the ulcerating types pain is the chief symptom.

On examination the growth may be seen projecting from the urethral orifice, or in other cases may be felt *per vaginam* as a line of induration along the urethra. Enlarged inguinal glands are found in about 20 per cent of cases at the first examination, though the enlargement may be due to secondary infection of the growth rather than metastasis. (It should be noted

that the lymphatics of the upper urethra also drain into the intrapelvic nodes). Biopsy is the final and essential step in diagnosis, sometimes with the aid of urethroscopy.

Treatment. Shaw¹⁷ has published a full review and no new principle can be added to his general account. As regards the primary tumour the choice between surgical excision and irradiation is obviously affected by the position and extent of the growth. If the posterior urethra is involved the growth can be excised only at the cost of permanent incontinence, although this can occasionally be overcome by suprapubic drainage if the bladder can be closed below (Battle¹⁸) or by ureteric transplantation. Irradiation has less operative risk, although there is a possibility of both fistula-formation and stenosis. The radiosensitivity of the growth varies with its type, and although it is generally stated that the squamous cell types are sensitive, there is less agreement about the columnar cell types. Radium needles can be inserted from above through the bladder as well as from below, if necessary. Radium has often been chosen for the more advanced cases, and this should be remembered when comparison with surgical results is made. The greater number of recent authors have preferred irradiation for the primary growth, employing interstitial radium, but the best plan would seem to be to treat each case individually, using irradiation for the more extensive growths, particularly of squamous cell type, and excising early growths, particularly those of the lower urethra. As biopsy is commonly necessary it would seem reasonable to excise a small tumour complete, rather than to remove a small part of it.

As regards the inguinal glands there is the same choice between surgical excision and irradiation, and here there is fairly

general agreement that surgery offers the best results. The nodes are often infected, and the overlying skin may not tolerate the large doses of radiation necessary to reach the glands in their fatty bed. Taussig¹⁹ has strongly advocated the Basset type of operation, even if the lymphatic nodes do not show clinical evidence of involvement.

It is difficult to draw definite conclusions about the choice of treatment from the literature, as the accounts given are so often inadequate, and also because of the short periods of follow up. Although individual accounts of success by many different methods can be found, the results in general are disappointing. Sparks and Parsons,¹⁴ for example, found only 15 survivors out of 119 after 3 years. Taussig's¹⁹ results are among the best, and his figures are especially valuable as they are based on an accurate follow up over 5 years. He reported 14 cases, and in 2 of these the disease was too advanced for treatment. Of the 12 cases treated 8 were treated by irradiation, with only 1 survival; 3 cases were treated by excision of the primary growth with Basset gland dissection, and all 3 survived; 1 other case was unsuccessfully treated by local excision alone.

Case Reports. Some apology is necessary for presenting these 3 cases, as the criticisms that I have made of other reports apply in part to mine, particularly as 1 case was followed for only 2 years. Furthermore, 2 cases were treated at a period of the war when radium was not available, and radon was used somewhat unscientifically.

CASE I.

A widow, aged 73, who had borne 1 child and had 1 miscarriage. Menopause at 50. She complained of bleeding "from the vagina" for 2 years. There had not been pain or urinary symptoms. On examination a soft vascular rounded tumour, 2 to 3 cm. in diameter, with a nodular surface was found attached to the posterior margin of the urethral orifice, and a deep submucosal extension was

spreading to surround the orifice. Soft inguinal glands were palpable, but not larger than are commonly felt. On October 3rd, 1941, the tumour and the adjacent tissues including the lower half of the urethra were excised, and it was possible to bring the mucosal edges together. Six radon seeds of 1.3 mc. were implanted around the operation site, and a catheter left in place. Bilateral dissection of the inguinal glands was performed.

Microscopical section showed an undifferentiated epidermoid carcinoma, with the cells arranged in large syncytial masses separated by scanty stroma. In other areas the cells were arranged more loosely presenting an appearance mimicking that of sarcoma. The hyperchromatic cell nuclei showed many mitoses. Most of the tumour was acutely inflamed and infiltrated with polymorphs. The inguinal lymph glands showed chronic inflammatory changes without evidence of metastasis.

After the operation the vulva and right leg became oedematous, but this soon subsided. The patient remained well for 2 years, but trace of her was then lost as she left London and did not answer letters.

This was a highly malignant and undifferentiated carcinoma and it is of interest that parts of the section mimicked sarcoma, though the growth as a whole was clearly a carcinoma, as a similar difficulty in diagnosis has been reported by Menville.²

CASE 2.

A widow aged 70, who had 3 children. Menopause at 47. She complained of bleeding at the end of micturition, for 2 weeks. There were no other symptoms. Five years previously a urethral caruncle had been removed. On examination an almost spherical vascular tumour 2 cm. in diameter was found at the posterior margin of the urethral orifice, and extending upward slightly into the canal. The mass was tender, firm in consistence, with a slightly nodular surface. Soft glands were palpable in both groins. Other pelvic abnormality was not found. On May 21st, 1941, the tumour was excised with a $\frac{1}{2}$ cm. margin of tissue, and 8 radon seeds of 1.3 mc. each were implanted around the operation site. It was possible to oppose the mucosal edges, and a catheter was left in place. The patient was frail, and in view of her age inguinal dissection was not performed.

The microscopical section showed tissue composed of fibrous and granulation tissue, with

marked superficial inflammation. There was extreme hyperplasia of the overlying stratified epithelium with marked activity of the cells suggestive of an early epithelioma, with infiltration at one point. The decision to leave the inguinal glands was supported by the relatively benign and early appearance of the growth.

The patient remained well for 3 years, but later in that year a local recurrence appeared, and she was admitted to Lambeth Hospital where she was treated with X-rays and by implantation of radon seeds, with retrogression of the growth. In April 1945 (4 years) there was no further evidence of recurrence.

This case was one of a very early squamous cell carcinoma, occurring at a site from which a caruncle had been removed 5 years previously. Although the tumour was 2 cm. in diameter, and presumably had been present for some time, the greater part of it consisted of granulation tissue, and the carcinoma itself was evidently very recent, possibly supervening on a pre-existing caruncle.

CASE 3.

This patient was under the care of Mr. A. J. Heriot and Mr. J. H. Peel and I am grateful to them for allowing me to include her. She was a parous woman aged 82, gravely ill on admission. She complained of pain in the lower abdomen and back of 1 week's duration, and of constant dribble of urine with haematuria. On examination the bladder was found to be distended up to the umbilicus, and attempts to pass a catheter failed because the distal urethra was surrounded by a submucous induration, which extended beneath the intact vaginal epithelium. The inguinal lymphatic nodes were not enlarged. Suprapubic drainage was established, and part of the growth excised for section.

The section showed sheets of carcinomatous cells, with a good deal of variation in size and shape, but mostly definitely squamoid, although without prickles or cell nests.

Fifty mg. of radium in a flat container with screenage equivalent to 3 mm. of lead was applied to the anterior vaginal wall and vestibule for 48 hours on 2 occasions. The growth retrogressed so that a catheter could be passed, but the patient's general condition remained precarious, and she died a month later. Permission for a postmortem examination was not obtained.

SUMMARY.

The literature on carcinoma of the female urethra is reviewed. Three new cases are reported.

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Fused Twin Monster

BY

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THE incidence of double monsters is low and the statistics of their occurrence are not particularly accurate. Mall¹ states that 7 per cent of all pregnancies terminate in aborted pathological ova and about 0.6 per cent in malformed fetuses at term; of the latter only a small proportion are conjoined twins. Puech² in 100,000 births found 517 malformations of various sorts, but of these only 2 were double monsters. Adair³ reported 2 double monsters in 25,000 deliveries at Chicago Lying-in Hospital. Mudaliar⁴ reported 4 double monsters between 1920 and 1928 among 25,000 deliveries and Rydén⁵ 2 thoracopagi in 40,000 births at Lund, Sweden, between 1900 and 1933. These figures can be compared with the rate of monozygotic twins which comprise 25 per cent of all twins; the ratio of all twins to single births being 1 to 85.2.

Joined-together twins may be described as human beings that have more than enough parts to make 1 individual, but not enough parts to make 2. Newman⁶ states that one-egg twins are the product of an incomplete twinning division symmetrically placed with respect to each other, i.e., one has developed from the right half of an embryo and the other from the left half. They are almost exact mirror-image duplicates. Double monsters are very rarely born alive because of the mechanical difficulties of delivery. "Siamese" twins are 2 nearly complete individuals and are therefore less monstrous, and cases of sur-

vival have been reported. The teratogenesis of the united twins has excited much interest and discussion; Ballantyne⁷ is inclined to accept the theory of polyspermy as the determining cause of these monstrosities. If two fertilizing spermatozoa gain entrance into the ovum, 2 primitive streaks, each with its own orientation, may be looked for; the proximity or separation of the primitive streaks will determine the relation of the future twins. The streaks may be in opposition to each other, when the craniopagous type of double monster may result; they may lie side by side, when thoracopagous twins will be produced; or they may be inclined towards each other at their anterior or posterior ends, when syncephalic or dicephalic terata will be formed. In all these monstrosities the twinship is the essential and original pathological fact.

CLINICAL HISTORY.

Mrs. H.S. was 19 years old when she attended this antenatal clinic with her first pregnancy. Her general health had always been good and there was nothing relevant in her past history. The last menstrual period was stated to be about August 18th, 1944, making the estimated date of delivery May 25th, 1945. She had married after conception occurred.

On examination she was seen to be anaemic, but other organic abnormality was not detected. The urine was free from abnormal constituents and the blood-pressure was 122/70. The pregnancy appeared normal for the period of amenorrhoea

until the 5th month. The pelvis was roomy. Between the 5th and 6th months the uterus became very tense and distended with numerous foetal parts. A provisional diagnosis of multiple pregnancy was made. Undue discomfort was not noticed until the 36th week, when she became dyspnoeic, had difficulty in getting about and developed mild toxæmia. She was admitted to hospital on May 4th, 1945. At this time there was generalized moderate oedema, a trace of albumin in the urine and the blood-pressure was 160/110. The abdomen was enormously distended and it was impossible to make out anything definite as hydramnios was present. An X-ray examination was carried out and the following report given: "Multiple pregnancy; twins; ? triplets; 2 presenting by the vertex; leading head appears deformed; ? dead foetus. Impossible to get a satisfactory A.P. view because of hydramnios. There are shadows in the lateral film which would do for 3 spines."

The toxæmia improved with rest in bed, but in view of the enormous abdominal distension and the fact that labour had not begun by June 2nd (1 week overdue by dates), the membranes were ruptured artificially and 5 pints of liquor amnii allowed to escape. The presenting part was very high and thought to be a face or anencephalic foetus. Four hours later good, regular contractions started and liquor drained abundantly from the vagina. On abdominal examination at this time doubt was felt as to the diagnosis of multiple pregnancy, as the whole abdomen was now soft without any apparent second bag of membranes. Limbs were easily palpable all over the abdomen, but a definite head could not be felt anywhere. A vague suspicion of fused twin monster was entertained, and it was decided to carry out a thorough vaginal examination after several hours of labour,

as the pelvis was very roomy. The cervix, however, dilated very rapidly, and 6 hours after the onset of labour pains it was fully dilated with what appeared to be a face presentation just inside the vagina. Under anaesthetic a full examination was made and showed a double face, with chin anterior, and an underdeveloped cranial vault. The forceps were applied and a fairly easy extraction of the fused anencephalic faces was achieved, with the aid of an episiotomy. The shoulders were difficult to deliver and the posterior arm was first brought down. Traction was then applied together with fundal pressure during the pains, the rest of the monster being delivered with ease.

The placenta was single and infarcted with only 1 set of membranes; it measured 9 inches in diameter. A moderate postpartum haemorrhage was controlled by oxytocic drugs and a hot intra-uterine douche. The patient made a good recovery.

The fused twin monster was stillborn¹ and weighed 8 pounds, the sex being female. See Figs. 1, 2 and 3.

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FIG. 1.

N.L.K.



FIG 2.

N L.K



FIG. 3.

N.L.K.

A Case of Sympus Dipus

BY

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SYMPUS dipus, or symmelia, is a foetal abnormality, characterized by the almost complete union of the lower extremities, and terminating in a double foot, the sole of which is turned to the front. In view of its constancy in almost all cases of sympus, and only in this type of monster, one other characteristic feature may be added, that is, as was first pointed out by Behn¹ in 1827, the presence in the umbilical cord of 1 vein, and a single artery.

Proshek² in 1925 was able to collect from the literature only 10 authentic cases of true sympus dipus reported since the year 1800, and described a case which occurred in the private practice of Dr. Fred L. Adair in 1923. Dreyfuss³ reported another case of this type in 1928, since when no other has been recorded.

The rarity of such a foetal malformation, and the tendency for such a foetus to adopt the breech position, makes the following case of interest.

A healthy primigravida, aged 24 years, visited the antenatal clinic for the first time when she was 16 weeks pregnant. The family history revealed the presence of 1 set of twins, a brother and sister, 2 years younger than the patient. There was no other significant fact in the history. On physical examination the uterus was found to correspond with the duration of amenorrhoea. The Wassermann reaction was negative, and the urine and blood-pressure normal.

An abnormality was not detected during the antenatal period until the 32nd week, when a breech presentation was palpated,

the foetal head being easily ballotted in the right hypochondrium. External cephalic version was attempted, but this was unsuccessful, owing to deep engagement of the breech in the pelvis. The patient was asked to come into hospital for version under anaesthesia on the following day. However, labour commenced prematurely, and an easy spontaneous delivery occurred 7½ hours later. The foetus, which weighed 3 pounds 15 ounces, and was 17 inches long, was born with its fused lower extremities extended over its abdomen, and died soon after delivery.

The foetus presented the following unusual features:

The lower extremities were completely united as far down as the toes, and were in a position of complete extension, a position which was maintained after delivery (Plate I). In the region of the knee joints, there was a faint linear depression, indicating the line of fusion of the limbs. Two femora, and two patellae were felt, the latter being directed postero-laterally, a small dimple on the right side marking the medial margin of the right patella.

The heels were fused and placed anteriorly, as were the plantar surfaces of the fused feet. Six toes were present, 3 on each foot. The external genital organs were not present, and there was no anal opening. The umbilical cord contained 1 vein and a single artery, which was found to communicate with the aorta directly, before its bifurcation.

X-ray examination showed 2 femora, and 2 fibulae on the inner aspects of the tibiae (Plate II).

Autopsy disclosed absence of the kidneys and ureters, marked distension of the lower gut, which appeared to enter a rudimentary bladder, that is, a persistent cloaca. A testicle was found on each side, in the inguinal canal. The upper extremities, chest, and head were normal.

This foetus hence exhibited all the classical features of true symphus dipus, according to the classification of St. Hilaire.⁴

COMMENTARY.

St. Hilaire⁴ in 1836 first classified foetal *abnormality of this type according to the extent of the union of the lower extremities into the following groups:*

(i) Symèle, in which the lower extremities are almost perfectly united, and terminate in a double foot, the sole of which is turned to the front.

(ii) Uromèle, in which the lower extremities are very incompletely united, and terminate in a double foot, usually very incomplete, the sole of which is turned to the front. According to Bennington,⁵ the limb may contain 3 bones, sometimes 2, and only 1 patella. In this class of foetus there is neither anus nor urinary tract. The external genital organs are usually present.

(iii) Sirénomèle, in which there is incomplete fusion of the lower extremities, which terminate in a stump, or in a point without a distinct foot. Bennington describes the foot as sometimes being represented by a toe, or rudiment of a toe.

Förster⁶ in 1861, introduced a classification, similar to that of Hilaire, merely altering the terminology, which is now generally used in the English literature. The symèle of St. Hilaire he called symphus dipus, the rarest of this type of foetal abnormality. The uromèle was called symphus monopus, and the sirénomèle symphus apus,

the commonest form of symphus according to Proshek.²

AETIOLOGY.

Four main theories are put forward to explain the causation of symphus dipus:

(1) Weigert⁷ and Kampmeier⁸ assume that the single artery in the umbilical cord is present in almost all cases of symphus, and only in this type of foetal monstrosity. They therefore conclude that this anomaly was the primary cause of such an abnormality. Weigert further believes that the fusion of the limbs and associated maldevelopments are only secondary, due to malnutrition as a result of impaired blood supply.

(2) St. Hilaire⁴ and Solger⁹ explain the fusion of the limbs by an approximation of the side plates from which the limbs are developed and as a result of that approximation, fusion takes place. St. Hilaire based his theory on the law of affinity, "like for the like." That is, the union was what he called a "natural" process, quite as natural a process as the union of other parts of the body, which at first lateral and paired, afterwards become united. The reason why the extremities do not as a rule unite, was because they do not have the opportunity of coming into contact.

(3) Gebhard¹⁰ and Gruvillier,¹¹ adopt the view that fusion occurred as a result of pressure, either by the amnion or by the uterus itself.

(4) Bolk¹² explains these monsters as being due to "mechanical" disturbances in the germ plasma.

DIAGNOSIS.

In no case was symphus dipus suspected before delivery in the cases mentioned above. In all but 1 case, hydramnios, which is usually expected in the presence of foetal malformation, was not present.



PLATE I.

Breech Delivery Sympus Dipus.

Note—Absence of rotation of hind limbs. Non-development of external genitalia and absence of anus.

L. R.



PLATE II

In a case of twins associated with hydramnios, described by Bauereisen, the first foetus presented all the features of true sympus dipus, the second infant showing atresia of the anus and rectum, the bowel ending blindly in the posterior wall of the bladder, and absence of one kidney. The cases reported by Bauereisen,¹³ Gladstone,¹⁴ Proshek,² Dreyfuss,³ and in this paper, were delivered as breech presentations. Details of the mode of delivery in the remaining 8 were not mentioned.

It appears therefore that the only aid to the diagnosis of such foetal monstrosities before delivery, is the location of the fibulae on the medial aspects of the tibiae, on radiological examination.

SUMMARY.

A case of sympus dipus is described, and the theories of causation outlined.

A possible aid to the diagnosis before delivery is suggested.

I wish to thank Mr. George Brown, Medical Superintendent to this hospital, for his permission to publish this case, and Sister Winters for the clinical photographs.

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BOOK REVIEWS

"The Premature Baby." By V. MARY CROSSE, M.D., D.P.H., M.M.S.A., D.R.C.O.G. 1945. 156 pages. Published by J. & A. Churchill, Ltd., London. Price 10s. 6d.

AFTER reading this book, one wholeheartedly reiterates the views of the writer of the foreword: "This book is unique in British literature."

By producing enlightening statistical tables the author adds weight to her invaluable suggestions for the reduction of mortality and morbidity among these babies. There is no doubt that it is the co-operation between obstetricians, paediatricians, general practitioners and midwives on the lines clearly indicated in this book which will help to bring about the reduction we desire.

Especial stress is laid on the dangers of infection. The value of penicillin is now apparent. Its lack of toxicity compared with the sulphonamides makes it often the drug of choice in the treatment of infections in premature babies, and this should be stressed in a subsequent edition.

More recent work appears to contradict the author's statement that the absence of immune agglutinins in the serum of a Rh negative mother carrying a Rh positive foetus means very little. We now know that in these cases the agglutinins may be fixed by the foetal blood. Again, there is now evidence that even hydrops foetalis may be compatible with survival if the infant is transfused at birth.

However, these are the only criticisms, constructive in intent, that can be made of a most valuable book whose widespread use is strongly recommended.

A. H. C. WALKER.

"Diagnostic Methods Used During the Later Months of Pregnancy and During Labour." (Fifth edition.) By J. C. WINDEYER, M.D., Ch.M. (Sydney), M.R.C.S. (England), L.R.C.P. (London), F.R.A.C.S., F.R.C.O.G. Professor

Emeritus, late Professor of Obstetrics, The University of Sydney. 1945. 32 pages. Sydney: Australasian Medical Publishing Co. Ltd. Price 2s.

IN this little book there is no attempt made to cover the subject of antenatal care. The purpose is to make the reader familiar with the bedside methods of examination to be used in late pregnancy and labour—viz. abdominal, vaginal and rectal examination and pelvimetry.

As might be expected emphasis is laid on abdominal examination. The best part of the book is that dealing with palpation of the abdomen. This is described in six steps:

- (1) The recognition of the foetal back.
- (2) Palpation of the anterior shoulder.
- (3) To verify the diagnosis of the position of the head.
- (4) To estimate the degree of flexion of the head.
- (5) Estimation of the relative size of the head and the pelvic brim.
- (6) Estimation of the approximate size of the foetus.

Palpation of the anterior shoulder, and estimation of the relative size of the foetal head and the pelvic brim are particularly well done. The course taken by the anterior shoulder in anterior and posterior positions receives careful consideration. The value of accurate shoulder palpation as a means of estimating progressive descent of the foetal head on the one hand, or arrest of descent on the other, is clearly described.

X-ray pelvimetry receives a brief mention. It is stated that this will become the rule rather than the exception in the near future. While the reader is reminded that one cannot foretell how the head will mould or how strongly the uterus will contract during labour, mention is not made of the necessity for *first class* radiological standards and accuracy, if this kind of pelvimetry is not to be misleading.

When discussing auscultation the author omits to point out that in extended breech presentation, with the breech deeply engaged, the maximal intensity of the foetal heart is to be found *below* the umbilicus.

Vaginal examination is described at length. Smooth gloves are advocated as causing the least discomfort and trauma, and diminishing the risk of carrying infected material upwards. Digital estimation of pelvic conformation, and the assessment of cephalopelvic proportion or disproportion, are described at length. But the necessity for the bladder being empty before this is attempted is not mentioned. Yet even Caesarean section has been performed unnecessarily because of such an omission.

Exception might be taken to the unqualified statement that rectal examination is without risk to the mother.

This little book is well worth reading. It is the attempt by an able clinician to inspire the attainment and maintenance of a high standard of clinical examination. Other special methods are relegated to their proper place—adjuvants to the clinical approach. It can be recommended to all who practise or wish to practise the obstetric art.

ANTHONY W. PURDIE.

"Human Embryology" (Prenatal Development of Form and Function). By Professors W. J. HAMILTON and J. D. BOYD, and Associate-Professor MOSSMAN. 1945. 345 pages. Cambridge: Heffers. Price 3s. 6d.

Books on human embryology have two uses: either to provide a reader with an account of the present state of our knowledge of human development and its relation to general biological principles; or to provide a medical student with as much of those matters as is of value to him in his studies and practice. It is the opinion of the writer of this review that it is impossible for anyone to write a book to serve both these ends successfully. A book which satisfies the first reader is one with full details of the subject, written in such a manner that comparison with other mammals or vertebrates is easy, with an ample bibliography and an assumption that the reader has already taken a course of comparative embryology and is conversant with the technical terms and practical methods connected with the subject. For, after

all, no one thinking to begin to study embryology seriously would start at the mammals. Before we can see how a textbook of embryology should be written for the benefit of those studying medicine, we must first decide the place the subject occupies in the curriculum, and, if we really face facts, we come to these conclusions. Certain facts of the subject are part of the essential knowledge of all general practitioners of medicine; the knowledge of certain others are part of the necessary mental equipment of various specialists; but the great bulk of the facts of human development have no permanent value to a graduate of medicine and many of them never have any value at all.

The subject is included in the course of anatomy because: (a) it explains the reasons for many facts of adult structure and therefore makes them easier to remember; (b) it explains many abnormalities which the student is bound to meet in the dissecting-room or operating theatre; (c) it makes the whole lay-out and structure of the body more intelligible and the study of it, therefore, more intelligent. Besides this it is educational, training one's visual memory and powers of three-dimensional visualization, as well as being informative and instructive on a subject which should be intensely interesting to anyone wishing to take up a medical career. But, with the exception of the facts mentioned above as part of the necessary equipment of a trained medical man, the subject is not included in the curriculum for its own sake, is not taught to students with a basic knowledge of vertebrate embryology and is not learnt so that students may become embryologists. In these circumstances a textbook of Human Embryology should be written in the plainest English, with the minimum of technical terms and scientific names which appertain only to embryology, and with no more detail than is consistent with truth and a sufficient presentation of the subject; sufficient, that is, to allow it to play the part in the curriculum indicated above.

Now it must be obvious that no book can be written to satisfy the needs of both these types of readers, because what is necessary for the first one makes the book unsuitable for the second. The book of which this is a review, however, attempts to satisfy both, and, as a result, will satisfy the student of embryology; but includes a chapter on Comparative Vertebrate Embryology, which he

will not find very useful. On the other hand, the medical student will find the bulk of the text overloaded with technical terms, language and detail, and containing much that will tend to hinder rather than help him. Considering the early stage in his university career at which he studies the subject, a glossary and a fuller index would have greatly added to the value of the book to him. The authors do not seem to have realized sufficiently how wide is the difference between their own learning and language and the knowledge of a second-year medical student, but, if they thought it necessary to write in such technical language and to introduce so many technical terms, they should have made it as easy as they could for the reader to find out the accurate meaning of the words used. (A word like "congenital" should be carefully defined whereas its meaning can only be incorrectly gleaned from the explanation given of "congenital disease." The introduction of the word "herniates" by putting it in brackets after the word "projects" and then the omission of any index reference to the page is another example.) The present reviewer, however, is one of those people who perhaps has a bee in his bonnet over what some writers call "jargon", and another might not be appalled by the fact that, in a very fully illustrated book of 345 pages, technical words or phrases are stressed by being printed in italics not far short of two thousand times.

But apart from these criticisms, which some people will not consider to be very serious, there is little but the highest praise to be given to the authors and their collaborators. The book is the most complete, the most splendidly illustrated, and, thanks to the inclusion of the findings of experimentalists, the most alive account of human development to date. I very much doubt whether a textbook of embryology will ever be better illustrated than this one: it is not simply that Mr. A. K. Maxwell is a master of his art and craft, but that the authors have appreciated how supremely important illustrations are and how numerous and well-chosen the figures must be to enable those unfamiliar with the subject fully to understand the text, however clearly that may be written. The text in this volume is, when one considers the amount of detailed information it contains and the complication of the subject, extraordinarily lucid and easy to read; and, altogether, the authors are

to be congratulated upon having produced a most valuable book and a most acceptable addition to any biological or anatomical library. It is as good as it well could be for a student of embryology who wishes to read a full and up-to-date account of the state of our knowledge of human development and well worth the guinea and a half (a very reasonable price for such a book even before the war) to a medical student, if only for the illustrations with which it is so abundantly adorned.

G. L. PURSER

"Control of Pain in Childbirth." By CLIFFORD B. LULL, M.D., F.A.C.S., and ROBERT A. HINGSON, M.D., with a Foreword by NORRIS W. VAUX, M.D. 1944. 356 pages. Philadelphia, London and Montreal: J. B. Lippincott Co. Price 7-50 dollars.

THIS volume of some 300 pages is, like most American publications, handsomely produced and beautifully illustrated with photographs and coloured diagrams. Perhaps this aspect of the book is overdone, for example, it is hardly necessary to use a full-page coloured diagram (Plate VII) to illustrate that in caudal anaesthesia the needle may be properly placed in the caudal canal or improperly placed in the periosteum or outside the sacrum.

The book opens with an excellent account of the anatomy of the nervous system and of the pelvis and its organs, and the pharmacology of various anaesthetic and analgesic agents. The bibliography is immense, and therefore as a book of reference the volume may be commended. But if the purpose of the authors, as one is led to believe, is to sift all the evidence and present it in a practical form, then I think there is something left to be desired. From the mass of material presented it would be difficult for anyone without wide experience to assess the value of any one method. Its claim, therefore, to be an aid to the general practitioner is doubtful. Indeed the general practitioner in reading the list of apparatus necessary to control pain in home delivery may wonder why the only item omitted is the pantechicon to convey it all.

The chief interest of the book is the account of caudal analgesia which is claimed to be the greatest advance so far in the control of pain in childbirth. It is claimed that in 40 to 60 per cent of cases the

force, frequency and duration of uterine mobility are not altered; but in nulliparae, because of loss of muscle power, low forceps will in most instances have to be applied. In 20 to 25 per cent uterine tone is diminished but the amplitude of contractions increased. In both these groups labour is said to progress rapidly and the level of analgesia does not proceed above the 9th thoracic segment. But there is a third group in which there is diminution of the amplitude of contractions, and in which, we are told, the analgesia may reach the 5th to the 1st thoracic segment; labour is ineffectual, and there is foetal (not to say maternal) anoxia!

The technique of administering caudal analgesia would be difficult and time-consuming enough in hospital practice where there is every facility for assistance and a good aseptic technique, but it is difficult to believe that it can be widely adopted in general practice unless the patients can afford the whole-time attendance of an anaesthetist and

obstetrician, or, shall we say, an obstetrico-anaesthesiologist.

A great part of the work would appear to be a treatise more on obstetrics than on anaesthesia. In a book purporting to discuss the control of pain in childbirth is it necessary to list Stroganov's theories on eclampsia, or the caution necessary in the selection of donors for Rh negative patients? And surely the section on X-rays of the sacrum and pelvis is outside the problem of anaesthesia. In the coloured photographs illustrating the actual birth of a child by natural or surgical means the mother is shown laughing appreciatively and wide-mouthed, unscreened from the field of operation; also, 75 per cent of her attendants have their noses uncovered! The style is a little verbose and sentimental and the book adds up as a textbook of obstetrics written by an expert in the use of caudal analgesia.

DOROTHY SPENCE SALES.

REVIEW OF HOSPITAL REPORT

THE CLINICAL REPORT OF THE NATIONAL MATERNITY HOSPITAL, DUBLIN, FOR THE YEAR 1944.

DURING the year there were 3,858 patients admitted to the maternity wards of the hospital. There resulted from these 3,187 intern-deliveries. This is an increase of 168 admissions and 185 deliveries on the previous year's figures. The result, according to the Master, is an overloading of the intern maternity service with the resultant evils of the shortened puerperium and incomplete establishment of breast feeding. As the number of beds in the maternity department is not stated it is not possible to estimate just how serious the overcrowding is.

In the first 17 pages there is a summary of the most important features of the report. The next 73 pages are concerned with detail. Here many conditions are set out case by case while others (e.g. breech delivery and delivery by the forceps) are summarized numerically in tabular form. Why these conditions should be selected for compression is not made clear. It is to be regretted in breech presentation. A distinction is not drawn between complicated and uncomplicated breech. The foetal mortality (3 stillbirths) in primigravid breech presentation (19 cases) is stated to be 15 per cent. What interests the obstetrician is the foetal mortality in uncomplicated primigravid breech delivery. This figure is obscure. But if we exclude 2 cases delivered by Caesarean section and 3 "associated with twins," then we have 3 stillbirths in 14 breech deliveries, i.e., 21 per cent.

Of 83 cases of persistent occipito-posterior position 29 were delivered by the forceps, 10 of these as unreduced posterior positions. Brow presentation deserves special mention. There were 8 (not 7 as stated) cases of brow presentation. All 8 were delivered by the vaginal route with 6 living infants (2 infants were stillborn, but in each case

the forceps had been applied unsuccessfully before the admission of the patient to hospital): there was no maternal death.

There were 4 cases of pubiotomy or symphysiotomy. Dr. Spain is convinced that these operations have a small but definite sphere of usefulness. He does not enlarge upon the indications for their use, but draws attention to the pelvic architecture of the subjects in which they were employed. In 3 the main feature was a narrow pelvic outlet. This indication is stressed by others who still find a limited place for these operations. In the 4th case there was narrowing of the mid cavity of an asymmetrical pelvis, due to inward bulging of an acetabulum. (Spelling in this section is rather eccentric.)

There were 17 cases of destructive operations on dead infants to facilitate delivery. These were mainly perforation of the foetal head. It is not made clear whether any difference is implied between "perforation of the head" and "craniotomy." There were 6 elderly primigravidae in this group and 4 of these had severe toxæmia. Caesarean section might have been preferable treatment. We are not told, however, which cases were "booked" and which were "emergencies" ("admitted at term in labour" might fall into either category.) It is difficult, therefore, to evaluate the line of treatment followed. There is no specific statement on the maternal result, save that 3 cases were morbid. While the presumption is that none died, the statement that 3 were morbid would be equally true if the 3 had died (B.M.A. standard).

There is a more liberal use of Caesarean section than formerly. There were 64 (not 63 as stated in the tables) cases of first Caesarean sections (including hysterectomies). It is stressed that all were lower segment sections. An arbitrary limit is not set to the number of repeat sections which can be carried out on the same individual provided they are lower segment operations, performed by

competent operators under good conditions. This view has allowed the more liberal use of the operation in the elderly primigravida, placenta praevia, toxæmia (for which 8 sections were performed), and certain other obstetrical conditions. There were 29 (not 30 as stated) "repeat" sections. There was 1 maternal death in the 93 cases. Except in a few cases of placenta praevia, the anaesthetic used for all sections was local infiltration with 0.5 per cent novocaine with, in addition, sufficient nitrous oxide and oxygen to allay the patient's anxiety. While there were no stillbirths, there were 8 neonatal deaths. In 5 of these the section was done for placenta praevia—in 3 (not 4 as stated) the child weighed less than 5 pounds. It is interesting to note that even though there were 5 neonatal deaths in the 20 cases of placenta praevia delivered by Caesarean section, in 10 cases of placenta praevia treated by Braxton-Hicks or internal version only 1 child survived.

The placenta was removed manually on 45 occasions. Most practising obstetricians would agree with the Master that, when haemorrhage is present, this is a simple and effective operation, provided it is done promptly while the patient's condition remains good. Doubtless the Master is equally right in his criticism that the blood transfusion situation in Dublin is unsatisfactory. In the only death in this series the removal was undertaken for retained placenta with postpartum haemorrhage. The patient did not have a blood transfusion. The cause of death was shock and haemorrhage.

The hospital morbidity on the B.M.A. standard is 1.78 per cent.

There were 17 maternal deaths. These are set out clearly in a table of some 6 pages. Four of these might be classed as 'avoidable'—1 case of puerperal sepsis in which many attempts at delivery before admission had failed; 1 of central placenta praevia when Caesarean section might

have been preferable to Braxton-Hicks' version and the bringing down of a leg; 1 rupture of uterus which occurred (in a case undergoing trial of labour) while preparations were being made for Caesarean section; and the case of postpartum haemorrhage already referred to, when blood transfusion might have saved her.

Brief reports follow on extern maternity cases, the infants', the gynaecological, the X-ray and the pathological departments.

This is not an easy report to read. The 17 pages of the summary are clear and interesting, but the tables of detailed cases make heavy reading. So much matter is contained under "remarks" that "summary of the case" would be a more accurate description. In spite of their being so long, information which would be of value is sometimes omitted, e.g., the degree of dilatation of the cervix when prolapse of the umbilical cord was first diagnosed. It seems undesirable to record in the tables under the heading "Result M.C." 'L' for a child which in fact died. An example of this is seen on page 45, Reg. No. 20850. Glancing quickly down the table it would seem that the result to all the children on that page was favourable. Only after reading a "remark", approximating to 40 words do we find out that the child whose "result" was said to be 'L' actually died. Why not record the result as 'N.D.' or 'Died' where it can be seen at a glance.

Even if somewhat heavy reading this is a most interesting report. Here we see reflected the outcome of vital thought. In this year's work we find the altering attitude to the elderly primigravida, placenta praevia, the severe toxæmia and Caesarean sections. That this is not mere change for the sake of fashion is to be gathered from Dr. Spain's remarks (page 16) on the subject of induction for suspect disproportion in the primigravida.

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the treated rats (Figs. 1 and 2). The vascular pattern is that of the normal immature uterus. The ovaries of injected and control rats show no difference in size or structure—the treatment has not promoted follicular stimulation, ovulation or corpus luteum formation (Figs. 3 and 4). Green-Armytage¹ after a like treatment records marked increase in size together with muscular hypertrophy and progestational changes of uteri of spayed immature rats. It is improbable that our failure to reproduce these positive responses could be attributed to the presence of the ovaries in our animals. It might, however, be suggested that the ovary antagonizes any hormonal action of semen, which of course would imply that it would have no effect on the normal adult female.

2. *Immature Rabbits.*

Two immature rabbits, one 8 weeks, the other 12 weeks old, were given an intravenous injection of 1 c.cm. of human semen in 3 c.cm. of saline on each of 3 days. There was no vaginal reaction during the experiment. They were killed 24 hours after the last injection, together with 2 control rabbits, one 8 weeks and the other 12 weeks.

Compared with the uteri of the control animals the treated uteri do not show any increase in size, endometrial or muscular hypertrophy, or any glandular hyperplasia. The vascular pattern is that of the immature uterus (Figs. 5 and 6).

There is no evidence of any stimulation or other effect on the ovaries (Figs. 7 and 8).

3. *Immature Guinea Pigs.*

Six immature guinea pigs (not litter mates) of weights ranging from 280 to 380 g. were given subcutaneous injections of 1 c.cm. of human semen on alternate days over a period of 20 days. There was no vaginal reaction during the period of the experiment. The animals were killed 2

days after the last injection along with 2 untreated guinea pigs of about 300 g. in weight.

Figs. 9 and 10 are sections of the largest and smallest uteri respectively. On the average there is some slight increase in the size of the uterus compared with the uteri of controls (Fig. 11) but no marked endometrial hypertrophy or signs of progestational changes. The vascular pattern is that of the immature animal and there is no evidence of the antimesometrial hyperaemia of the "oestrous" uterus.² The ovaries do not show any sign of stimulation—in both treated and control animals there are large secondary follicles in the ovaries.

4. *Immature Guinea Pigs.*

Six immature guinea pigs (not litter mates) of weights ranging from 280 to 380 g. were given subcutaneous injections of 2 mg. testosterone propionate on alternate days over a period of 30 days.

During treatment there was hypertrophy of the clitoris in all the animals. The vaginae opened in 2 animals (in Animal No. 1 on the 9th day and remained open for 5 days—in Animal No. 3 on the 3rd day for 24 hours) and the vaginal smears were dioestrous (leucocytic). The animals were killed 3 days after the last injection.

Compared with the uterus of the control animal (Fig. 12) there is a more marked increase in size than in the semen-treated animals. The uterine reaction is, however, far short of the response of the immature uterus to oestrogenic therapy,⁴ nor are there any progestational changes. The vascular pattern is that of the normal immature uterus. In the ovaries there is no evidence of follicular stimulation, but there appear to be more follicles with commencing atretic change.

5. *Adult Spayed Guinea Pigs.*

Treatment commenced 8 weeks after operation. Six animals were given a sub-

cutaneous injection of 1 c.cm. of human semen every alternate day over a period of 20 days. There was no vaginal reaction. The animals were killed 2 days after the last injection, along with an untreated spayed adult as a control. Figs. 13 and 14 show sections of the largest and smallest uterus. Apart from one animal there is no increase in size as compared with the uterus of the control animal (Fig. 15) and no marked hypertrophy or progestational change. The vascular pattern is that of the dioestrous uterus.

6. *Adult Spayed Guinea Pigs.*

Treatment was commenced 8 weeks after operation. Six animals were given subcutaneous injections of 4 mg. of testosterone propionate on alternate days over a period of 20 days.

In all the animals there was hypertrophy of the clitoris. In half the animals the vaginae opened and dioestrous (leucocytic) smears were obtained. Animals were killed 2 days after the last injection. In all the animals there is a definite increase in the size of the uterus when compared with that of the control animal (Fig. 16) but no marked progestational changes. In one animal (Fig. 17) the uterine response is comparable to that obtained in the spayed animals following oestrogenic stimulation.³ In this animal the greatly enlarged uterus has a dilated lumen, enlarged hypertrophic glands, antimesometrial hyperaemia and all the display of the oestrous uterus.

DISCUSSION.

Injection of semen into immature rats and rabbits yields completely negative results and does not afford any evidence of hormonal activity in semen. In the immature and adult spayed guinea pigs after semen injections there appears to be an increase in the size of the uterus but this requires cautious interpretation. The 6

immature guinea pigs were of varying ages and sizes and their uteri therefore in different stages of immaturity, while the degree of involution of the uteri of spayed adult animals is a variable factor. Moreover, such small responses might be due to some non-specific protein reaction of no particular gynaecogenic significance.

There was no significant difference in the size, number or condition of the ovarian follicles of the control and treated animals. We have to conclude, therefore, that semen has no gonadotropic action.

It is perhaps not unnatural to assume that semen possesses a hormone allied to testosterone, for which, however, there is no experimental confirmation. Parallel experiments with testosterone and semen provide a useful comparison. "Male" effects, for example, hypertrophy of the clitoris and preputial glands, were found only after testosterone treatment and never following semen injections. Vaginal opening with leucocytic smears is a female manifestation of testosterone and could not be evoked by semen.

There are many conflicting observations on the effect of testosterone on the rodent uterus. Korenchevsky, Dennison and Eldridge,³ Korenchevsky and Hall,⁶ and Noble⁷ record marked progestational changes in the uteri of spayed adult rats but McKeown and Zuckerman⁸ were unable to produce such changes after similar experiments. Deanesly and Parkes⁹ have noted an increase in the size of the uterus following testosterone treatment, while Phelps, Burch and Ellison¹⁰ conclude that the response of the endometrium of the guinea pig uterus to testosterone and theelin is qualitatively similar.

With the exception of 1 animal we did not find any progestational changes in the immature or adult spayed guinea pig uteri after testosterone injections and although there was a definite uterine hypertrophy,

DESCRIPTION OF PLATES

(All illustrations are untouched photomicrographs)

Owing to the very considerable variation in the sizes of the uteri of the different species of experimental animals it was not possible to use the same magnification throughout and therefore a comparison should not be made of the sizes of the uteri of rat, rabbit, and guinea pig. The same magnification was, of course, used for the photographs of the uteri from animals of the same group.

PLATE I

- FIG 1 Uterus of immature rat after semen injections. No evidence of oestrogenic or progestational change $\times 100$
 FIG 2 Uterus of untreated litter mate $\times 100$
 FIG 3 Ovary of immature rat after semen injections. No evidence of ovarian stimulation $\times 74$
 FIG 4 Ovary of untreated litter mate $\times 74$

PLATE II

- FIG 5 Uterus of immature rabbit after semen injections. No increase in size, no muscular or endometrial hypertrophy $\times 32$
 FIG 6 Uterus of untreated control of the same age $\times 32$
 FIG 7 Ovary of immature rabbit after semen injections. No evidence of ovarian stimulation $\times 120$
 FIG 8 Ovary of untreated control of the same age $\times 120$

PLATE III

- FIGS 9 AND 10 Uteri of immature guinea pigs after semen injections. Fig 9 represents the largest and Fig 10 the smallest uterus of the group of 6 treated animals. Slight increase in size but no marked endometrial hypertrophy $\times 45$
 FIG 11 Uterus of untreated control approximately of the same age $\times 45$
 FIG 12 Uterus of immature guinea pig after testosterone propionate administration. Definite increase in size furthermore the uterus with its wider lumen has lost its immature appearance. Cf Fig 11 $\times 45$
 FIGS 13 AND 14 Uteri of spayed adult guinea pigs after semen injections. Fig 13 represents the largest and Fig 14 the smallest uterus of the 6 treated animals. Apart from some general increase in size there is no marked endometrial hypertrophy or progestational change $\times 22$
 FIG 15 Uterus of an untreated spayed adult control $\times 22$
 FIGS 16 AND 17 Uteri of spayed adult pigs after testosterone administration. Fig 16 represents the smallest and Fig 17 the largest uterus from the group of 6 treated animals. In Fig 17 the uterine response is comparable to that obtained in the spayed animals following oestrogenic stimulation. Cf figures with Fig 13 $\times 22$

FIG. 1



FIG. 2

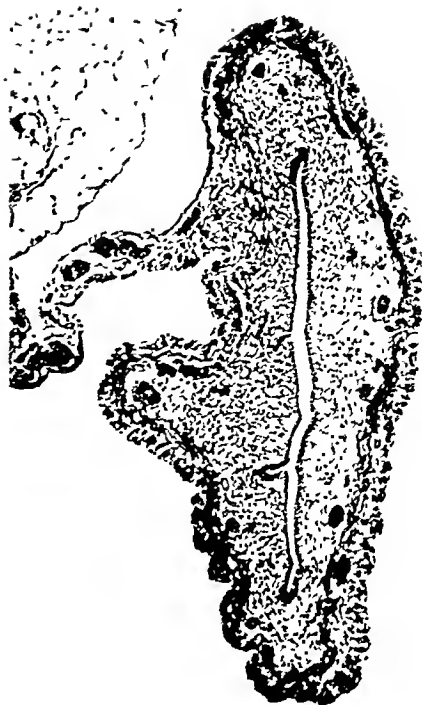


FIG. 3



FIG. 4

PLATE III

FIG. 9



FIG. 10



FIG. 11



FIG. 12

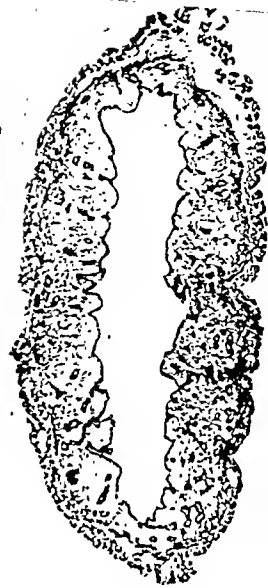


FIG.
14



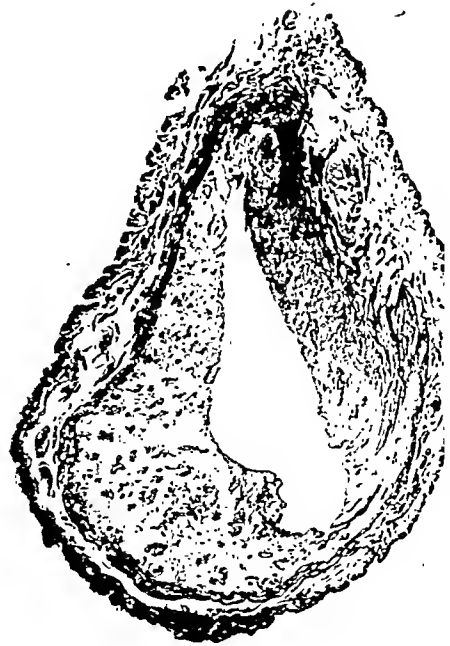
FIG. 15



FIG. 13



FIG. 16



it compares unfavourably with the results obtained after oestrogenic stimulation'. The weight of evidence for and against the gonadotropic action of testosterone is about equal and is reviewed by Korenchevsky,¹¹ Noble,⁷ and Robson.¹² We could not find any evidence of any stimulating (gonadotropic) effect on the ovaries from testosterone. The variety and range of the responses of the female to testosterone propionate treatment, which have been recorded in different animals under many experimental conditions, would make it hazardous to predict the results in any given instance of testosterone propionate therapy in the female.

From our experiments we are of the opinion that the final development of the uterus is not a function of semen and further that semen does not possess the biological qualities of testosterone, nor is it probable that testosterone could be entrusted to ensure uterine maturation. In this connexion it has recently become apparent that both male and female sex hormones are present in the female organism and a number of the 17 ketosteroids have been recovered from the female urine. Callow and Callow¹³ found androsterone and transdehydroandrosterone in the normal female urine in amount comparable to that obtained from the urine of the normal male. If therefore "male" hormone is necessary to promote full uterine development it is already available in the female.

It has been suggested elsewhere¹⁴ that the inability to induce in immature animals by hormonal treatment all the uterine changes necessary to maintain pregnancy, and the relative sterility of adolescence are but different aspects of the same fundamental problem. What Mirekaya and Crew¹⁵ refer to as the lack of some "essential contribution from the immature soma" is manifest in the inability of the immature uterus to respond maturely to hormonal

stimulation. This would imply that delayed maturation may exist along with a normal hormonal balance. Reynolds¹⁶ is of the opinion that uterine tissue has to accustom itself to periodic hormonal activity and that there is a time of experience during which it acquires the optimal capacity for pregnancy. In our view the gradual transformation of the stubbornly immature into the mature uterus is more likely to be a function of time than the perquisite of the male. Coitus of course may cause reactions independent of the presence or absence of semen in the vagina, for example, postcopulatory ovulation in rabbits, and these results, which are concerned only with the activity of semen, do not exclude the possibility that sexual union may produce effects from reflex nervous stimulation.

SUMMARY.

1. A series of injections of human semen were given to immature rats and rabbits. There was no vaginal reaction during the experiments, no evidence of oestrogenic or progestational change of the uterus and no ovarian stimulation.
2. Injections of human semen were given to immature guinea pigs. There was no vaginal reaction. On the average there was a slight uterine hypertrophy but this was not regarded as significant. No evidence of ovarian stimulation.
3. Injections of testosterone propionate were given to immature guinea pigs. In all the animals there was during treatment, hypertrophy of the clitoris and in 2 guinea pigs the vaginae opened and dioestrous smears were obtained. There was uterine enlargement, more marked than in the semen-treated guinea pigs but far short of the response of the immature uterus to oestrogenic therapy. There were a greater number of atretic follicles in the ovaries.
4. Injections of human semen were given to spayed adult guinea pigs. There

was no vaginal reaction during treatment. There was, on the average, some slight increase in the size of the uterus but this was not regarded as significant.

5. Injections of testosterone propionate were given to spayed adult guinea pigs. During treatment there was hypertrophy of the clitoris in all animals, half of which also showed vaginal reaction in the form of vaginal opening and dioestrous smears. There was a definite uterine enlargement but in only one animal was the uterine response comparable to that obtained in spayed adult guinea pigs after oestrogenic stimulation.

ACKNOWLEDGEMENTS.

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The Influence of Social and Economic Factors on Stillbirths and Neonatal Deaths*

BY

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PREMATURITY.

IN a previous paper¹ the importance of prematurity as a cause of stillbirth and neonatal mortality in Social Classes III, IV and V of the community has been brought out. It is now proposed to examine the probable causes of prematurity, basing the discussion on the *data* already presented.

Definition.

The term prematurity is used here to include all infants of $5\frac{1}{2}$ pounds or less irrespective of the duration of gestation. In some cases the pregnancy had reached full time by dates, but the child was classified as premature by weight.

The League of Nations Medical Committee (1936) suggested the use of the weight basis if the pregnancy had reached the 28th week. Recently Henderson² suggested that infants below 2 pounds 12 ounces (1,250 g.) weight should not be included, but should be regarded as abortions or pre-viable, but since some infants of this weight survive and many live for days, they can hardly be classified as abortions. There is a better case for having a lower weight limit for stillbirths.

INCIDENCE OF PREMATURITY.

General Review.

The incidence of prematurity is difficult to obtain because of the difficulty of accu-

ate weighing in domiciliary practice. In New York State (1936) the incidence of prematurity was estimated to be 4.3 per cent. In New York City (1940) the incidence was 7 per cent. In Chicago the incidence as estimated by Bundesen³ was 0.5 per cent. In Birmingham in 1943⁴ the figure was 6.3 per cent. Hospital figures, while they give much information about premature infants not available in domiciliary practice, do not represent a typical cross section of the community. Chicago Lying-in Hospital (1940) had a prematurity-rate of 5.6 per cent, and this seems fairly representative of American hospitals. In Britain, hospital figures are much higher than this. Queen Charlotte's Hospital had an incidence of 8.11 per cent⁵; in booked cases it was 6.78 per cent, and in emergency cases 27.2 per cent. The incidence in hospital will depend upon the proportion of emergency cases treated. In the Aberdeen Maternity Hospital (1941-2) the incidence of prematurity was 13.4 per cent; (booked cases 8.8 per cent, emergency cases 39.4 per cent).

Aberdeen Study.

In the following investigation booked hospital cases only have been considered—Group 2. These have been compared with nursing home cases—Groups 1 and 3. During the years 1938-44, 8,808 booked cases were treated, and in 738 instances labour resulted in a premature baby according to the above definition (8.38 per

* Continued from p 234 of June issue

cent). There were 798 babies of 5½ pounds or less, 8.97 per cent of the total infants born—see Table I. The incidence of pre-

TABLE I.

Causes of Prematurity in 738 Cases out of 8,808 Booked Hospital Cases.
(6 years' data).

GROUP 2.

| Cause of onset of premature labour | Number | Per cent of total premature labours |
|--|--------|---|
| Cause unexplained | 383 | 51.9 |
| Accidental haemorrhage (with- out toxæmia) | 29 | 3.9 |
| Eclamptic toxæmia | 119 | 16.1 |
| Twin pregnancy (including 15 cases of toxæmia) | 90 | 12.2 |
| Gross foetal deformity | 25 | 3.4 |
| Placenta prævia | 20 | 2.7 |
| Syphilis | 19 | 2.6 |
| Severe maternal heart disease | 19 | 2.6 |
| Miscellaneous | 34 | 4.6 |
| Total premature labours | 738 | 8.38 per cent of the total deliveries |
| Total cases of prematurity | 798 | 8.97 per cent of the total babies |

maturity in cases booked under the domiciliary midwifery scheme during the years 1942-43 was 7.4 per cent. The patients belong to the same social class as the hospital cases, and when the two groups are taken together it brings the incidence of prematurity in "working class" practice to 8.1 per cent. During the years 1938-44 there were 1,419 deliveries in the nursing home group (Group 1), with 71 premature infants, 5 per cent. If the incidence of prematurity for all the other cases not born in hospital or under the domiciliary scheme be 5 per cent, which is a low estimate, the

total prematurity-rate for the City would be about 7 per cent. In the group of 501 specialist cases, Group 3, the incidence of prematurity was 4 per cent (20 cases—1 stillbirth and 19 live births). There is a much greater incidence of prematurity in working-class practice than in the nursing home groups.

Tables II, III and IV show an analysis by weight of the cases of prematurity in each group. They show that not only is the incidence of prematurity greater in Group 2 cases, but the proportion of very small babies is greater. The mortality in the premature infants in Group 2 is 257 per 1,000 compared to 119 in Group 1. Excluding the premature stillbirths, the weight group 5½ to 4½ pounds contains 75 per cent of the Group 1 cases, and 62 per cent of the Group 2 cases. In Group 1, 6.8 per cent of the premature infants weighed 3½ pounds or less, while 16.3 per cent of the Group 2 cases were of this weight. It is well known that the mortality in premature infants varies with the birth weight. In the weight group 5½ to 4½ pounds the mortality in Group 2 cases was 106 per 1,000 compared with 45 per 1,000 in Group 1. In the weight group 4½ to 3½ pounds the mortality in Group 2 cases was 294 per 1,000, and in Group 1, 91 per 1,000. Not only, therefore, is the incidence of prematurity in Group 2 much higher than in Group 1, and the proportion of very small infants greater, but for the same weight the mortality in Group 2 is twice or three times that of Group 1. This difference is due to the fact that the infants in Group 1 are much more vigorous and begin to gain weight more quickly than those in Group 2; it is not due to a better standard of nursing and medical care. There are no special facilities for nursing premature infants in the nursing home where Group 1 infants are born comparable to those available in the maternity hospital for Group 2. This dif-

TABLE II.

Weight Distribution and Mortality in 59 Live-born Premature Infants in Group 1, out of 1,419 Cases.

| Weight in pounds | ... | 5½-5 | 5-4½ | 4½-4 | 4-3½ | 3½-3 | 3- | Total |
|-------------------------|-----|------|------|------|------|-------|-----|-------|
| Lived | ... | 26 | 16 | 8 | 2 | 0 | 0 | 52 |
| Died | ... | 0 | 2 | 1 | 0 | 2 | 2 | 7 |
| Per cent of total cases | | 44.1 | 30.5 | 15.2 | 3.4 | 3.4 | 3.4 | 100 |
| Mortality per 1,000 | | 45 | | 91 | | 1,000 | | 119 |

TABLE III.

Weight Distribution and Mortality in 626 Live-born Premature Infants in Group 2.

| Weight in pounds | | 5½-5 | 5-4½ | 4½-4 | 4-3½ | 3½-3 | 3- | Total |
|-------------------------|--|------|------|------|------|------|-----|-------|
| Lived | | 233 | 114 | 60 | 36 | 17 | 5 | 465 |
| Died | | 27 | 14 | 17 | 23 | 36 | 44 | 161 |
| Per cent of total cases | | 41.5 | 20.4 | 12.3 | 9.4 | 8.5 | 7.8 | 100 |
| Mortality per 1,000 | | 106 | | 294 | | 784 | | 257 |

TABLE IV.

Weight Distribution and Mortality in 19 Live-born Premature Infants in Group 3.

| Weight in pounds | | 5½-5 | 5-4½ | 4½-4 | 4-3½ | 3½-3 | 3- | Total |
|-------------------------|--|------|------|------|------|------|----|-------|
| Lived | | 3 | 9 | 2 | - | 2 | - | 16 |
| Per cent of total cases | | 2 | 0 | 0 | - | 1 | - | 3 |
| Mortality per 1,000 | | - | - | - | - | - | - | 158 |

ference in vitality must be taken into account when comparing the mortality figures from different parts of the country and different social groups. It is more likely to explain the great difference in mortality recorded by Crosse in Birmingham and by Field in London (quoted by Parsons⁶) than differences in methods of feeding or nursing. Crosse's results are similar to those in Aberdeen Group 2, and probably refer to the same social class. In both groups the proportion dying of infection (theoretically avoidable) was about 10 per cent; about 70 per cent of the deaths occurred within a short time of birth, and these deaths are largely unavoidable at the moment, despite the most modern hospital facilities.

ETIOLOGY OF PREMATUREITY.

Unfortunately not enough information is available about the health of the mothers in Group 1 during pregnancy to give a list of the causes of the prematurity in this group. Table V gives a list of the maternal conditions responsible for the onset of premature labour in Group 3, and, except in 3 cases out of 20, the cause was well defined and due to a well-recognized obstetrical condition. Table I gives a list of the causes of the onset of premature labour in Group 2 and their relative frequency. In 51.9 per cent the cause of the prematurity could not be explained. This is in direct contrast to the findings in Group 3 which, although numbers are small, show that only 3 out

20 cases came into this category. There is therefore a striking difference in etiology between the 2 groups. In the one group the premature labours are nearly all due to well-recognized obstetrical causes, while in the other more than half of them are unexplained. When the cases are analysed according to the date of confinement it is found that in 19 per cent of the cases of unexplained prematurity in Group 2 the pregnancy had reached 40 weeks, and was, therefore, full-time by date. In 34 per cent of cases the pregnancy had reached 38 weeks. Therefore in about one-third of these cases of unexplained prematurity the problem seems to have been more an interference with the growth and nutrition of the foetus rather than the premature onset of labour. In Group 3 there were 2 out of 20 cases of prematurity full-time by date, and in both cases the mothers' health seemed good during pregnancy. It will be shown later that many of the women in Group 2 are small themselves and have small babies, for example, 13.8 per cent of them are under 5 feet in height, and in this group 34 per cent of the babies are between 5½ and 6½ pounds in weight.

Table VI is an analysis of 338 consecutive cases of unexplained prematurity in Group 2, arranged according to age and parity, and it shows that unexplained prematurity is slightly more common in primiparae than multiparae, and it increases with age after the age of 24. Pregnancies repeated too frequently result in increased frequency of prematurity. For example, the rate in the 3rd, 4th and 5th pregnancies under 24 years was 5.9 per cent, while in women of 30 to 34 it was only 3.9 per cent. In the 6th, 7th and 8th pregnancies in women between 25 and 29 it was 8.1 per cent, in women 10 years older it was 3.6 per cent. Numbers are so small that reliable conclusions on the point cannot be reached. Very few of these

women were in what could be described as poor health, and few had any complaint. The general appearance of the primigravidae was usually much better than that of the multiparae, and yet they showed a higher incidence of prematurity.

The tendency to prematurity of unknown cause is more common in women who have had previous premature babies. For example, in 81 women who had 1 previous pregnancy 20 (25 per cent) had an unexplained premature baby and 16 per cent had had an abortion previously. In a group of 82 having had 2, 3 or 4 previous pregnancies 31 (38 per cent) had had previous premature babies, 12 (15 per cent) had previous abortions. Some had as many as 2 or 3 premature babies. Out of 25 women who had 5 or more previous pregnancies 17 (68 per cent) had had either a previous premature baby or an abortion.

Since Group 2 corresponds roughly to Classes III, IV and V of the Registrar

TABLE V.
Shows the Causes of Prematurity in 20 Cases out of 501 Specialist Cases. (Group 3.)

| | | | | |
|-------------------------------|-----|-----|----|-------------|
| Eclamptic toxæmia | ... | ... | 13 | (9 induced) |
| Severe maternal heart disease | ... | ... | 2 | |
| Full time by dates | ... | ... | 2 | |
| Anxiety state | ... | ... | 1 | (induced) |
| Gross foetal deformity | ... | ... | 1 | |
| Unknown cause | ... | ... | 1 | |

General's classification and Groups 1 and 3 to Classes I and II, it is clear that unexplained prematurity is relatively common among the poor and uncommon among the well-to-do. It must therefore be related to social and economic conditions.

With regard to the recognized obstetrical causes of prematurity Table I shows that eclamptic toxæmia is the most common because of spontaneous or induced premature onset of labour. Table VII shows that the incidence of prematurity due

TABLE VI.

Prematurity 'Cause Unexplained,' Including Premature Stillbirths in Hospital Booked Cases (Group 2) by Parity and Age Group.

| Age distribution | | | | | | | | | | | | | | |
|------------------|-----|----------|-----|----------|-----|----------|-----|----------|-----|----------|-----|----------|-----|----------|
| — 20 | | 20-24 | | 25-29 | | 30-34 | | 35-39 | | 40 + | | Total | | |
| Parity | No. | Per cent | No. | Per cent | No. | Per cent | No. | Per cent | No. | Per cent | No. | Per cent | No. | Per cent |
| 1 | 27 | 4.7 | 59 | 4.0 | 38 | 5.1 | 18 | 6.1 | 8 | 7.2 | — | — | 150 | 4.7 |
| 2 | 4 | 5.8 | 31 | 4.6 | 26 | 3.9 | 13 | 4.2 | 6 | 5.7 | 1 | — | 81 | 4.1 |
| 3, 4, 5 | — | — | 19 | 5.9 | 30 | 4.3 | 20 | 3.9 | 9 | 4.0 | 3 | 1.6 | 82 | 4.5 |
| 6, 7, 8 | — | — | — | — | 8 | 8.1 | 2 | 1.1 | 6 | 3.6 | 2 | 1.1 | 18 | 3.5 |
| 9+ | — | — | — | — | 1 | — | 3 | 0.0 | 3 | 3.5 | — | — | 7 | 1.0 |

TABLE VII.

Shows the Incidence of Prematurity Due to Eclamptic Toxaemia in 7,476 Consecutive Cases in Group 2 by Age and Parity. (5 years' Data).

| Age of mother | — 20 | | | 20-24 | | | 25-29 | | | 30+ | | | All ages | | |
|-------------------------|------|------|------|-------|------|------|-------|------|------|------|------|------|----------|------|------|
| | No. | ture | cent | No. | ture | cent | No. | ture | cent | No. | ture | cent | No. | ture | cent |
| No previous pregnancies | 562 | 12 | 2.1 | 1458 | 18 | 1.2 | 739 | 21 | 2.8 | 401 | 17 | 4.2 | 3160 | 68 | 2.2 |
| Previous pregnancies | 68 | 0 | 0.0 | 999 | 3 | 0.3 | 1455 | 7 | 0.5 | 1794 | 17 | 0.9 | 4316 | 27 | 0.6 |
| All pregnancies | 630 | | | 2457 | | | 2194 | | | 2195 | | | 7476 | 95 | 1.3 |

o toxaemia is more than 3 times as great in a first pregnancy as in subsequent pregnancies. It also rises with age after the age of 24 years. Unfortunately the incidence of prematurity due to toxaemia in Group 1 cannot be compared with Group 2 since the necessary clinical details are not available. Group 3, which is much smaller, is available, however, for comparison. There were 13 cases of prematurity due to toxaemia in this group (Table VI), an incidence of 2.0 per cent compared to 1.3 per cent in Group 2. This higher incidence of prematurity in Group 3 is due to its unfavourable age and parity distribution. Tables II and IX show these 2 groups arranged by parity and age to show the incidence of eclamptic toxaemia. The total incidence was 4.4 per cent in Group 3 and 8.5 per

cent in Group 2. In the age group 25 to 34 in primiparae in Group 2 the incidence of toxaemia was 3 times that of the same age group in Group 3. The incidence of eclamptic fits was 0.59 per cent (17 cases of eclampsia in 2,890 cases) in Group 2, and 0.20 per cent (1 out of 501 cases) in Group 3. It has been shown that pre-eclamptic toxaemia is the most common cause of prematurity in Group 3 (65 per cent of the total in Group 3 as against 16.1 per cent in Group 2), and despite this the incidence of pre-eclampsia is only slightly more than half that in Group 2. This fact, plus the absence of prematurity of unknown causes, explains very largely the difference in prematurity-rates between the two groups.

Twin pregnancy is the next most common cause of prematurity in Group 2. In

TABLE VIII.

Incidence of Eclamptic Toxaemia in 2,890 Consecutive Cases in Group 2 by Age and Parity.
(2 years' data.)

(Only those cases having Oedema or Albuminuria as well as Raised Blood-pressure are included.)

| Age of mother | -24 | | | 25-34 | | | 35+ | | | All ages | | |
|-----------------------|--------------|----|----------|--------------|----|----------|--------------|----|----------|--------------|-----|----------|
| Parity | No. Toxaemia | | Per cent | No. Toxaemia | | Per cent | No. Toxaemia | | Per cent | No. Toxaemia | | Per cent |
| No previous pregnancy | 886 | 85 | 9.6 | 422 | 61 | 14.5 | 64 | 10 | 15.6 | 1372 | 156 | 11.4 |
| Previous pregnancy | 340 | 12 | 3.5 | 899 | 57 | 6.3 | 279 | 22 | 7.9 | 1518 | 91 | 5.9 |
| | | | | | | | | | | 2890 | 247 | 8.5 |

TABLE IX.

Incidence of Eclamptic Toxaemia in 501 Specialist Cases in Group 3 by Age and Parity.

| Age of mother | -24 | | | 25-34 | | | 35+ | | | All ages | | |
|-----------------------|--------------|---|----------|--------------|---|----------|--------------|---|----------|--------------|----|----------|
| Parity | No. Toxaemia | | Per cent | No. Toxaemia | | Per cent | No. Toxaemia | | Per cent | No. Toxaemia | | Per cent |
| No previous pregnancy | 56 | 5 | 8.9 | 199 | 9 | 4.5 | 45 | 3 | 6.7 | 300 | 17 | 5.7 |
| Previous pregnancy | 10 | 0 | 0.0 | 133 | 2 | 1.5 | 58 | 3 | 5.2 | 201 | 5 | 2.5 |
| | | | | | | | | | | 501 | 22 | 4.4 |

7,514 consecutive cases in Group 2 (5 years data) twins occurred 79 times, an incidence of 1 in 95 births. The incidence was 1 in 118 in the 1st pregnancy and 1 in 63 in the 6th pregnancy onwards. During the years 1942-43 there were 2,890 booked hospital cases in Group 2, and twins occurred on 44 occasions (1 in 65 births). Of these 88 twins 63 were premature weighing 5½ pounds or less (72 per cent) distributed as follows:

| | |
|-------------------|----|
| 5½ to 4½ pounds | 31 |
| 4½ to 3½ .. | 14 |
| 3½ pounds or less | 18 |

There were 5 stillbirths and 17 neonatal deaths, giving a combined mortality of 25 per cent. In Group 1 out of 1,419 cases twins occurred on 14 occasions (1 in 101 births). Of the 28 babies 9 were premature weighing 5½ pounds or less (32 per cent), distributed as follows:

| | |
|-------------------|---|
| 5½ to 4½ pounds | 5 |
| 4½ to 3½ .. | 4 |
| 3½ pounds or less | 0 |

There was no stillbirth and only 1 neonatal death—a combined mortality of 3.6 per cent. The combined total stillbirth and neonatal mortality in Group 1 was 38.3 per 1,000, and in Group 2, 64.9 per 1,000, an excess over Group 1 of 69 per cent. In the case of twin pregnancy on the other hand, the mortality in Group 2 is more than 6 times that in Group 1. The other causes of prematurity are too small numerically for comparison to be made between the 2 groups.

Several recent publications agree in general with the observations made here. Crosse¹ found that in 37.7 per cent of a total of 924 premature births an adequate explanation could not be found for the onset of labour, and in one-third of the cases a history was given of 2 or more premature

or miscarriages. Sandifer,⁵ in a study of 1,000 cases of premature labour, found that the cause of the premature onset was explained in 37.2 per cent. The proportion of emergency cases, as was done in the above series of cases, would increase the proportion of premature labour due to conditions as toxæmia and placental infarction and other recognized obstetrical causes of premature labour, so that for the selected cases which are much more likely to represent a cross section of the area studied by the hospital the proportion where the onset was unexplained might be in the neighbourhood of 50 per cent.

SUMMARY AND CONCLUSIONS.

The conclusion to be drawn from these figures is that in Scotland the incidence of prematurity is greater than in England, and that in the Scottish cities and maternity hospitals greater than in the hospitals and cities in England and America. In a previous paper it has been shown that the mortality from prematurity is higher in Scotland than in England and Wales or Holland, and that the excess of neonatal mortality in Scotland is due largely to the excess mortality from prematurity. It has been shown that prematurity is almost twice as high in social Classes III, IV and V as in Classes I and II. In the former classes 50 per cent of the prematurity is unexplained; in the latter very few are in this category. The most common obstetrical condition associated with prematurity is eclamptic toxæmia, and this is twice as common among the poor as the well-to-do for the same age and parity group. In Classes III, IV and V, as represented by Group 2 in this paper, twin pregnancy is a great strain, and, judging from the cases studied in this series, the foetal mortality is 6 times that of Classes I and II. The most likely explanation of these differences is

that in Group 2 the health and nutrition of the mother is inferior to that of the women in Groups 1 and 3. In Group 2 there are great variations since some obviously living at a low economic level have large families with no premature infants or abortions while others have repeated abortions or premature labours. This suggests that some women are much better able to utilize the food they eat than others. This in turn may be dependent on growth and general nutrition in early years rather than on diet during the pregnancy.

NUTRITION.

General Considerations.

We have shown that when hospital "booked cases" probably corresponding to Social Classes III, IV and V are compared with cases in private practice, Social Classes I and II, a much greater proportion of babies born are feeble. This shows itself in more unexplained stillbirths and more neonatal deaths due to congenital debility and atelectasis. There is a high incidence of prematurity which increases both the stillbirth and the neonatal mortality-rates. The great difference in the vitality of the offspring between the classes is hidden to some extent by the fact that in the hospital patients the age and parity distribution is much more favourable. In the pre-war years it has been shown by Orr⁷ and others that as the income rises the amount spent on food rises and the diet improves. The consumption of bread and potatoes is practically uniform throughout the different income level groups. Consumption of milk, eggs, fruit, vegetables, meat and fish rises with income. Thus in the poorest group the average consumption of milk including tinned milk, is equivalent to 1.8 pints per head per week; in the wealthiest group 5.5 pints. The poorest group consume 1.5 eggs per head per week; the wealthiest 4.5. The

poorest spend 2.4 pence on fruit; the wealthiest 1 shilling and 8 pence. The average diet of the poorest group, comprising 4,500,000 people (10 per cent of the population, expending on the average 4 shillings per head per week on food) is by the standard adopted deficient in every constituent examined. The 2nd group comprising 9,000,000 people (20 per cent of the population spending 6 shillings per head per week on food) is adequate in protein but deficient in all the vitamins and minerals. The 3rd group, 9,000,000, spending 8 shillings per week on food, is deficient in vitamins and minerals. Therefore 50 per cent of the population has a diet inadequate for full health. This 50 per cent contains about two-thirds of the children. As income increases, disease and death rate decrease, children grow more quickly, adult stature is greater and general health and physique improve.

Surveys have shown that in Scotland before the war there was twice as much poverty as in England, unemployment was greater and slums and squalid living conditions were much more common. Common observation shows that there are striking differences in physique and nutrition between the women seen at hospital antenatal clinics and those seen in private practice. There are differences in stature, the state of the teeth and gums, the condition of the hair and skin, the incidence of anaemia and the general air of vitality. These differences are difficult to measure accurately, however. Chemical tests for nutritional deficiency are difficult to carry out; even haemoglobin estimations can be misleading unless care is exercised. It is known that anaemia is common in pregnant women.¹

The teeth of women attending hospital antenatal clinics are much worse than those of women in private practice, and artificial teeth are much more common. This might

be due to some extent to less care of the teeth and the practice of extraction rather than filling.

The height of the patient is easily taken, and gives some idea of the nutritional state in the years of growth. In 1883 the British Association Anthropometric Committee showed that the average height of boys of 13½ years in an industrial school was 2.6 inches below that of artisan boys of the same age, and 5.8 inches below that of boys of the professional classes. Yudkin^{9, 10} recently demonstrated in Cambridge that children from smaller families were taller and heavier and had a higher haemoglobin level and a stronger grip than children from larger families—these differences being greater in the children from poorer areas. He also found that the nutritional state of the children and mothers was better in those who had more to spend. For example, when the sum available for food was between 7 shillings and 3 pence and 10 shillings and a penny per head per week, the children were on the average 1½ inches taller and 6 pounds heavier than those in families with a possible food expenditure between 4 shillings and 7 pence and 7 shillings and a penny.

Height of Mother in Relation to Weight of Baby.

The heights of four groups of expectant mothers have been compared, those attending (a) a relatively expensive nursing home, (b) a nursing home where the fees are less, (c) "booked" cases at the Aberdeen Maternity Hospital and (d) "booked" cases at the Glasgow Maternity Hospital. The results are seen in Fig. 1, and they show that the percentage of the women in each group who are less than 5 feet in height increases from 1.6 in group (a) to 26.8 per cent in group (d). Conversely the percentage of women who are 5 feet 6

inches or more diminishes from 24 per cent in group (a) to 3.3 per cent in group (d). In group (a) modal height is between 5 feet 5 inches and 5 feet 6 inches, in group (b) between 5 feet 4 inches and 5 feet 5 inches, and in groups (c) and (d) between 5 feet 2 inches and 5 feet 3 inches.

In the same city, therefore, there are differences of about 3 inches in the height of two groups of expectant mothers selected only on the basis of the expense of the confinement. It seems reasonable to assume that the women in group (c) would have grown these extra inches if their nutrition had been better in childhood. When the women in group (c) were divided into two groups, those under 25 years of age and those over 35 years, no evidence of increase in height among the younger women was noticed. In a small group of cases in which the grandmother was measured as well as the mother, the grandmother was found to be taller than the mother in half the cases. It might have been expected that the younger women would have been taller in view of the improving state of health of the community, but possibly some of the grandmothers were reared in the country and came to live in the city, where the nutritional level fell.

When the weights of the babies in the two groups are compared, it is found that in group (a) 9.2 per cent and in group (c) 18.8 per cent weigh between $5\frac{1}{2}$ and $6\frac{1}{2}$ pounds and in group (a) 39.2 and in group (c) 40.2 per cent weigh between $6\frac{1}{2}$ and $7\frac{1}{2}$ pounds. In group (a) 33.1 per cent and in group (c) 29.7 per cent weigh between $7\frac{1}{2}$ and $8\frac{1}{2}$ pounds. In group (a) 18.3 per cent and in group (c) 11.1 per cent weigh over $8\frac{1}{2}$ pounds. The babies in group (a) are therefore heavier on the average than those in group (c).

Each group was next analysed to see what relation, if any, existed between the height of the mother and the size of the

baby. The results are seen in Figs. 2 and 3. They show that in groups (a) and (c) the weight of the baby increases with the height of the mother. In (a) there are not enough patients under 5 feet in height to analyse, but thereafter, as the mother increases in height, the proportion of large babies (over $8\frac{1}{2}$ pounds) rises from 10 per cent to 29.6 per cent. In group (c) in which the mother is less than 5 feet in height 34 per cent of the children are between $5\frac{1}{2}$ and $6\frac{1}{2}$ pounds in weight. The proportion falls to 9.1 per cent when the mother is 5 feet 6 inches and over. Conversely when the mother is under 5 feet in height 5.5 per cent of the babies are over $8\frac{1}{2}$ pounds. When the mother is 5 feet 6 inches or over, 13.7 per cent of the babies are over $8\frac{1}{2}$ pounds. Thus there are many more large babies in group (a), 29.6 per cent with mothers of 5 feet 6 inches or more over $8\frac{1}{2}$ pounds in weight, compared to 13.7 in group (c). It is likely that in both groups (a) and (c) women of 5 feet 6 inches and over have reached their maximal height, so that the increase in the weight of the babies in group (a) may be related to better diet during pregnancy. When women between 5 feet and 5 feet 2 inches in height, or between 5 feet 3 inches and 5 feet 5 inches in the 2 groups are compared, less difference in the weight of the baby is seen. Some of the women in group (c) are much smaller than they might have been had they been well fed as children. If there are hereditary factors operating to produce big babies to big mothers, which seems likely from a study of group (a), then this acting in group (c) would tend to produce a larger baby than the height of the mother or her nutrition during pregnancy would lead one to expect. This factor might explain why at the height 5 feet to 5 feet 2 inches in group (c) 11.9 per cent of the infants are more than $8\frac{1}{2}$ pounds, while in group (a) only 10 per cent exceed $8\frac{1}{2}$ pounds. There is no

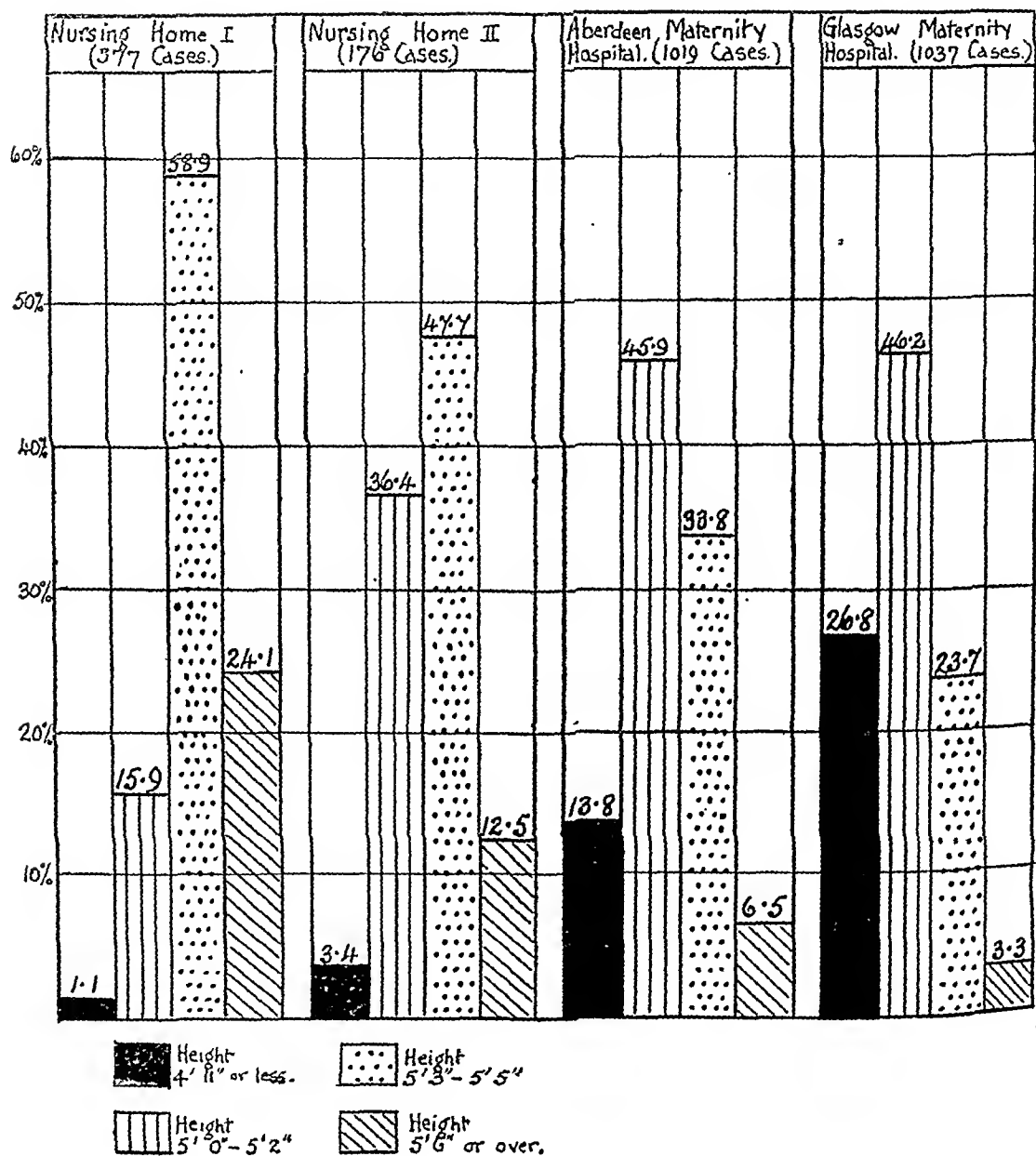
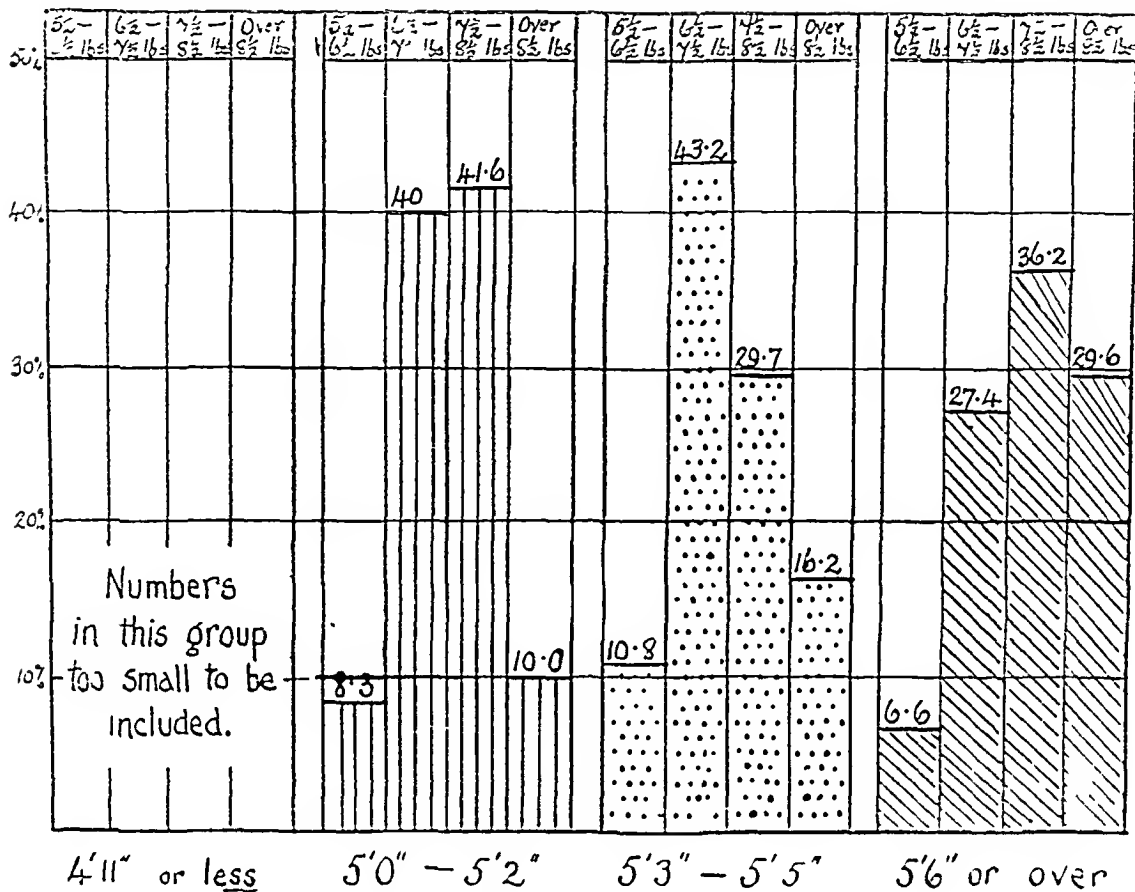


FIG. 1.

Comparison of heights of mothers in two nursing homes and in two maternity hospitals.



(i) Nursing Home I.

FIG. 2

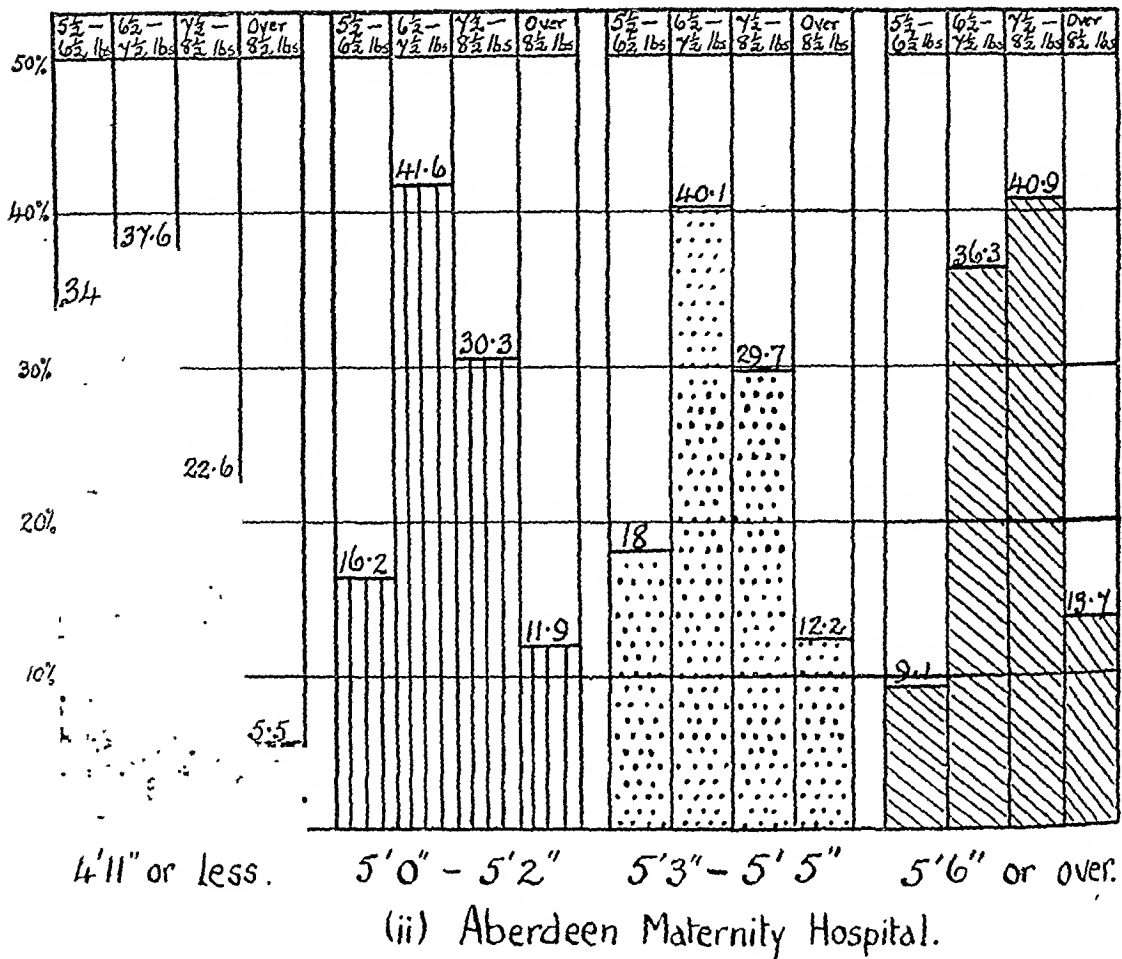


FIG. 3

Comparison of weights of baby in relation to height of mother in: (i) Nursing home, and (ii) Aberdeen Maternity Hospital (See also Fig. 2).

was very good. Table X shows that in the Glasgow Maternity Hospital (d) in women under 5 feet in height 19.4 per cent were delivered by Caesarean section, and in the Aberdeen Maternity Hospital (c) the percentage was 4.3. The forceps-rate was higher in (c) than in (d), possibly because there was such gross contraction of the pelvis in group (d) that Caesarean section was necessary while in group (c) the contraction of the pelvis was less severe and

forceps delivery was possible instead. The high forceps delivery rate in group (a) is due to the fact that the forceps is applied much more frequently in private practice, apart from any evidence of maternal or foetal distress. There is plenty of evidence that in the areas where there is a high incidence of rickets a high stillbirth-rate exists. This is probably not due to the high stillbirth-rate in cases of contracted pelvis so much as to the fact that the rickets is accom-

TABLE X.

Shows the Mode of Delivery in: (a) Nursing Home Cases, (c) Aberdeen Maternity Hospital 'Booked' Cases, (d) Glasgow Maternity Hospital 'Booked' Cases.

| | Group (d) | | | | Group (c) | | | | Group (a) | | | |
|------------------------------------|-------------------|----------|---------|----------|-------------------|----------|---------|----------|-------------------|----------|---------|----------|
| | Caesarean section | | Forceps | | Caesarean section | | Forceps | | Caesarean section | | Forceps | |
| | No. | Per cent | No. | Per cent | No. | Per cent | No. | Per cent | No. | Per cent | No. | Per cent |
| Under 5 feet | 12 | 10.4 | 19 | 8.8 | 141 | 4.3 | 23 | 16.3 | 4 | 2 | 2 | 50 |
| 5 feet to under 5 feet 2 inches | 10 | 2.9 | 29 | 8.1 | 468 | 1.1 | 49 | 10.5 | 60 | 2 | 21 | 35 |
| 5 feet 2 inches to 5 feet 4 inches | 3 | 1.0 | 17 | 5.8 | 344 | 0.9 | 31 | 9.0 | 218 | 0 | 63 | 28.9 |
| 5 feet 4 inches to 5 feet 6 inches | 2 | 0.0 | 1 | 3.4 | 66 | 0.0 | 8 | 12.1 | 91 | 0 | 37 | 40.7 |
| All heights | 54 | 6.9 | 66 | 8.1 | 1019 | 1.4 | 111 | 10.9 | 373 | 4 | 123 | 33.0 |

panied by other signs of poor physique and health. In the periods 1939-41 the stillbirth-rate in Greater London was 30, in Aberdeen 36 and in Glasgow 44. It has been shown that the women attending the hospital clinics in Aberdeen are taller than those in Glasgow. The contrast between Glasgow and London can be gathered from the experience of Kenny¹¹ and MacLennan.¹² The former found only 5 cases of typical rickety pelvis in 10,000 hospital patients in London. Only 1 of these was a London woman; the other 4 came from the depressed areas of the North, Clydeside, South Wales and Ireland. MacLennan, on the other hand, in Glasgow found 15 per cent of 1,049 suffered from contracted pelvis. Kenny dealt almost exclusively with anomalies in the shape of the pelvis while MacLennan disregards this as being relatively unimportant in Glasgow in view of the large amount of contraction due to rickets. Kenny had 35 stillbirths or early neonatal deaths out of 1,000 cases of difficult labour. This is no more than the stillbirth-rate for the whole country, and only 1 of these deaths was attributed to trauma, whereas MacLennan had a stillbirth-rate alone of 107 in cases of contracted pelvis, and when those delivered by Caesarean section are excluded, the stillbirth-rate for those delivered by the vaginal route was 222. The Glasgow Maternity Hospital admits many emergency cases, so that these figures cannot be used as a cross section of the country, but they give some indication of the amount of rickets, and by implication the amount of poor health and physique. A similar indication comes from a study of 1,000 children. According to Gray and others¹³ the per cent of rickets in Glasgow is 1.5, taken as the low figure of 1.5 per cent, the incidence should be about 1.5 per cent. The incidence in Glasgow is 1.5 per cent. The incidence in Glasgow is 1.5 per cent.

cent. He concludes that at least one-quarter of the infants admitted to the Sick Children's Hospital in Glasgow suffer from some degree of rickets.

Maternal Diet.

During 1942 a record was made by Cameron and Graham¹⁴ of the food intake of 300 women attending the Glasgow Maternity Hospital, made up as follows: 100 mothers of stillborn infants; 100 mothers of premature born infants, and 100 mothers of full-time infants. The average daily calorie intakes in these groups were 1,644, 1,710 and 1,946 respectively. The diet of the mothers with full-time infants was superior in every respect, particularly in first-class protein, calcium and phosphorus.

The diets of a series of 500 women attending the antenatal clinic at the same hospital were supervised during the last 3 months of pregnancy. To serve as contrast the records of 500 women attending the antenatal clinic during the same period, but whose diets were not supervised, were used. Both groups were "booked" cases. In the supervised group there were 21 stillbirths and 31 premature labours. In the control group there were 36 stillbirths and 50 premature labours. In the supervised group 357 infants were breast-fed at the time of dismissal, while in the control group only 276 were breast-fed.

The fact that in the control group the stillbirth-rate was equivalent to 72 and the prematurity-rate was 10 per cent, demonstrated the poor state of nutrition of the women attending the clinic. The fact that the diets varied from 1,644 calories to 1,946 calories shows how far they fell short of the optimum of 2,500. Even the stillbirth-rate of 42 in the supervised group is high since the stillbirth-rate for 1943 for the whole of Scotland was 36. Graham draws attention to the ignorance of many of the

patients with regard to food values and nutrition generally. It is scarcely surprising therefore that the stillbirth-rate in Glasgow during this time was 44. The report of the Joint Council of Midwifery,¹⁵ the paper of Ebbs, Tisdall and Scott,¹⁶ and the survey of the People's League of Health¹⁷ all point in the same direction, namely to the importance of nutrition in the prevention of stillbirths and premature labour. The great difficulty about experiments in human nutrition is that if careful dietary surveys are made, only small numbers can be dealt with, which makes it difficult to draw conclusions as to stillbirth-rates. If large numbers are taken, it is difficult to obtain accurate *data* about food intakes, and it is difficult to ensure adequate controls.

THE WAR YEARS.

Stillbirth-rate.

Since the war began there has been a striking fall in the stillbirth-rate in both England and Wales and Scotland. In England and Wales the stillbirth-rate in 1928-30 was 40. In 1936 the rate was still 40. By 1939 it had fallen to 38. In Scotland stillbirths did not become notifiable till 1939, in which year the rate was 42. For 10 years till the war, therefore, there had been very little change in the stillbirth-rate in England, and it is possible that in Scotland the rate was also stationary. Since then the stillbirth-rate has fallen steadily in both countries, in England from 38 to 28 (provisional) in 1944, and in Scotland from 42 in 1939 to 32 in 1944. In England analysis shows that this fall affects all age groups and all parities. For example, between 1938 and 1942 the stillbirth-rate in legitimate births to women under 25 fell from 27 to 24, between 25 and 34 years from 34 to 30, from 35 years onwards from 56 to 47. In first births the rate

fell from 41 to 34, and in a 9th pregnancy and over it fell from 62 to 56.

In Scotland (Table XI), the stillbirth-rates are shown for legitimate births in 1938, and in brackets after them are the corresponding figures for 1943. They show that there has been a fall in each age group and in each parity. This has been remarkably uniform, and it suggests some national factor which has operated since the war and not before it. The most likely factor is

natal and infant mortality, and one of the first attempts made to make such an analysis was that of the Registrar General for Scotland in his annual report for 1939. In Table XXVIII he makes a detailed analysis of 3,832 stillbirths with a total stillbirth-rate of 42.3, and he makes the following comments: "Of the broad groups, the largest number is contained in the ill-defined and unknown. Of the total 3,832 stillbirths, the cause is ill-defined in 901 and is stated to be

TABLE XI.
*Stillbirths (Legitimate) per 1,000 Children Born, by Age of Mother and
Number of Previous Children, 1938.*
(Figures in brackets, 1943.)
(Annual Report of Registrar-General for Scotland, 1939.)

| Number of previous children | Age of mother | | | | | | |
|--------------------------------|---------------|----------|---------|---------|---------|---------|-------------|
| | All ages | Under 20 | 20-24 | 25-29 | 30-34 | 35-39 | 40 and over |
| 0 | 49 (36) | 29 (19) | 37 (27) | 48 (35) | 62 (52) | 98 (73) | 95 (72) |
| 1 | 30 (25) | 32 | 21 | 29 | 35 | 46 | 38 |
| 2 | 32 (31) | 19 | 16 | 27 | 45 | 42 | 60 |
| 3 | 41 (35) | — | 27 | 31 | 44 | 58 | 80 |
| 4 | 43 (41) | — | 35 | 25 | 45 | 61 | 60 |
| 5 | 43 (52) | — | 25 | 30 | 38 | 52 | 72 |
| 6 | 53 (49) | — | — | 35 | 38 | 66 | 78 |
| 7 | 59 (57) | — | — | 30 | 33 | 68 | 91 |
| 8 | 58 (77) | — | — | — | 48 | 49 | 96 |
| 9 | 61 (57) | — | — | — | 26 | 66 | 82 |
| 10 and over | 86 (97) | — | — | — | 30 | 106 | 90 |
| Total | 42 (35) | 29 (19) | 29 (24) | 36 (28) | 46 (39) | 62 (54) | 77 (76) |

the improvement in the national diet among the poorer sections of the community who contribute most of the children. It has been suggested that the fall is due in part to the younger age of marriage, but an analysis of Aberdeen figures fails to show any significant change in the age grouping of the women having children during the war years, so that this factor probably plays a very small part in the fall in the stillbirth-rate. Figure 4 shows that the stillbirth-rate has fallen in the large cities in Scotland especially since 1942, with the exception of Dundee.

National figures for causes of stillbirths are not available such as those for neo-

unknown in 362 cases. Part of this high proportion of ill-defined and unknown causes is, no doubt, due to the novelty of the scheme and will doubtless be reduced as the value of specification of stillbirths by cause becomes apparent. For instance, in the group of ill-defined causes, 341 are ascribed to asphyxia, some of which are probably due to difficulties of delivery of various kinds; macerated foetus (175), of which in some cases the cause (toxaemia, syphilis, etc.) may have been known to the certifier. It will be noted that the 362 cases in which it was definitely stated that an obvious cause was not apparent represent nearly one-tenth of all stillbirths. If no

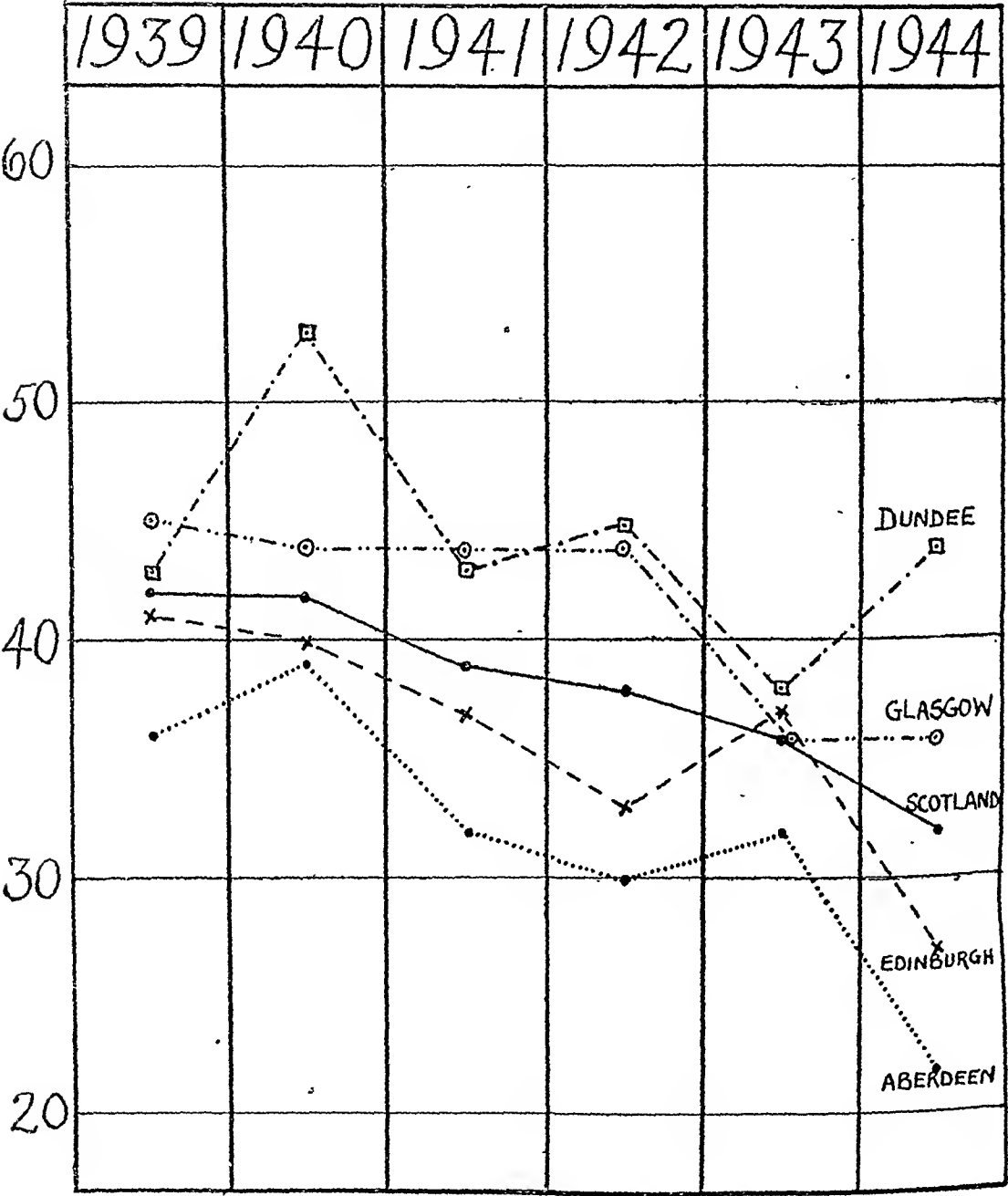


FIG. 4

Shows the stillbirth-rate in Scotland and the four large cities during the war years.

large part of this group is attributable to detectable causes, and therefore not likely to be reduced by more accurate recording on the certificate of the cause of death, the size of the group is of itself evidence sufficient to show the need for investigation of the factors leading to stillbirth before any hope of improvement can be entertained."

In "Infant Mortality in Scotland,"¹¹ an attempt is made to divide the 3,832 stillbirths referred to above into those due to the hazards of birth and those due to conditions pre-existing at birth, and it was found that 38 per cent could be classified as hazards of birth and 62 per cent due to conditions pre-existing at birth. In view of the absence of published national figures the Aberdeen figures have been analysed in much the same way for the war years to see in which categories the fall in the death-rate has occurred. The details of cases in 1939 are not available, but since then fairly accurate *data* are available, since a high proportion of stillbirths occur in the maternity hospital where postmortem examination is performed as a routine, and care is taken to collect clinical *data* about those dying at home or in nursing homes. The first point which is apparent from Table XII is that if the experience in Aberdeen is typical of Scotland as a whole, the estimate that 38 per cent of stillbirths are due to hazards of birth is too high. It is more probable that not more than 25 per cent of stillbirths are due to hazards of birth and 75 per cent are due to conditions pre-existing at birth. Table XII shows that when the mortality in 1940 is compared with 1944 there has been a striking fall in the number of stillbirths due to unknown factors, trauma and toxæmia. The only other cause of stillbirth which is important numerically is that due to foetal deformity, and here the fall in mortality has been much less. The remaining groups are too variable and too small in numbers to have

any conclusions drawn from them. Forty cases are included in the group inter-current disease and miscellaneous, and they were grouped as follows: syphilis 12, severe anaemia 6, diabetes 4, bowel complication 6, influenza and pneumonia 3, complications of twins 3, severe heart disease 2, pyelitis 2, Rh factor 2. Despite postmortem examinations and fairly accurate certification, 33 per cent of the total stillbirths in the 5 years are classified as "cause unknown," and this is the biggest individual group. The mortality in this group has been reduced by nearly 50 per cent, so that this represents a big saving in infant lives. The most likely explanation of this is better nutrition of the mother. The reduction in the death-rate from toxæmia has been just as great, and from trauma very considerable, although it must be remembered that in the neonatal period there has been no fall in the death-rate from trauma. The stillbirth-rate due to trauma among those delivered in hospital as booked cases has fallen, and in those delivered outside the hospital or admitted as emergency cases, there has been a similar fall in the death-rate from trauma. It may be that the fall in the stillbirth-rate from trauma is to some extent due to improved management of pregnancy and labour, but it seems more likely that it results from better nutrition of the mother, acting by improving the vitality of the infants so that they stand up better to the strain of difficult labour. It has been shown that toxæmia is less common in the better nourished section of the community, so that the fall in the stillbirth-rate due to toxæmia may again be due to improved nutrition of the mother.

Neonatal Mortality.

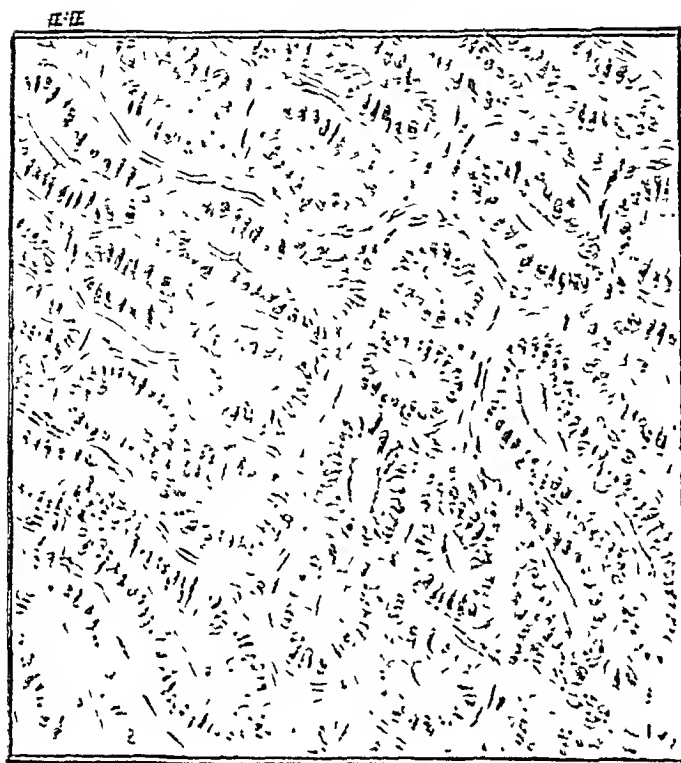
In contrast to the steady fall in the stillbirth-rate throughout the war years the neonatal mortality in both England and

TABLE XII.

| Causes of stillbirth | 1940 | | 1941 | | 1942 | | 1943 | | 1944 | | Total | No. of stillbirths | Per cent of total | 1944 as percentage of 1940 |
|-------------------------------------|------|----------------------------|------|----------------------------|------|----------------------------|------|----------------------------|------|----------------------------|-------|--------------------|-------------------|----------------------------|
| | No. | Death-rate per 1000 births | No. | Death-rate per 1000 births | No. | Death-rate per 1000 births | No. | Death-rate per 1000 births | No. | Death-rate per 1000 births | | | | |
| Cause unknown | 36 | 12.8 | 41 | 14.1 | 26 | 8.9 | 32 | 11.1 | 20 | 6.7 | 155 | 33.4 | 52 | |
| Trauma | 26 | 9.3 | 17 | 5.8 | 21 | 7.2 | 17 | 5.8 | 17 | 5.7 | 98 | 21.1 | 61 | |
| Toxaemia | 16 | 5.7 | 14 | 4.8 | 19 | 6.5 | 17 | 5.8 | 8 | 2.7 | 74 | 15.9 | 47 | |
| Accidental haemorrhage | 5 | 1.7 | 7 | 2.4 | 7 | 2.4 | 8 | 2.7 | 5 | 1.7 | 32 | 6.9 | 100 | |
| Deformity | 12 | 4.2 | 11 | 3.7 | 14 | 4.8 | 10 | 3.4 | 10 | 3.4 | 57 | 12.3 | 81 | |
| Miscellaneous intercurrent diseases | 13 | 4.6 | 5 | 1.7 | 5 | 1.7 | 14 | 4.8 | 3 | 1.0 | 40 | 8.6 | 22 | |
| Placenta praevia | 4 | 1.4 | 3 | 1.0 | 0 | 0.0 | 1 | 0.3 | 0 | 0.0 | 8 | 1.7 | — | |
| All causes | 112 | 39.9 | 98 | 33.7 | 92 | 31.6 | 99 | 33.9 | 63 | 21.1 | 464 | 99.9 | 52 | |
| Total births | 2804 | | 2907 | | 2904 | | 2889 | | 2989 | | | | | |

Section stained with haematoxylin and eosin. $\times 200$

FIGURE 2.



Section stained with Sudan IV. $\times 200$.

FIGURE 3.

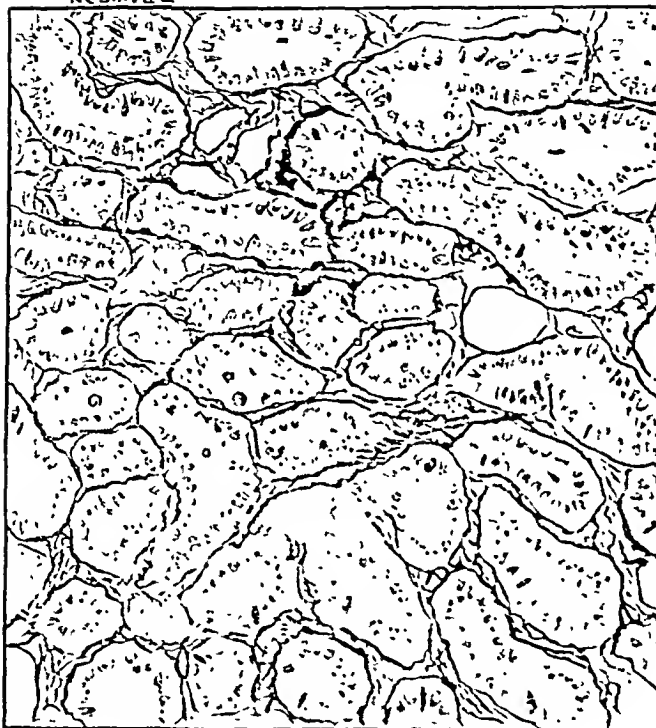


112

Silver stain to show reticulum. $\times 200$.

Figure 4.

J. DAVISON.



histological picture was quite different, as under a low power the tumour was seen to consist of an encapsulated mass of perfectly-formed tubules more or less divided up into lobules by incomplete septa well supplied with blood-vessels. Lying over part of the circumference of the tumour and outside the capsule were the remains of the ovary proper containing Graafian follicles in various stages of development, a number of corpora albicantia but no recent corpora lutea. The general arrangement of tumour and ovary suggested that the tumour had not originated in the ovarian cortex but in the medulla or hilum.

Haematoxylin and eosin, Sudan IV and a silver stain were used to demonstrate the microscopic anatomy.

In sections stained with haematoxylin and eosin (Fig. 2), the tubules were seen to be fully differentiated and to consist of a single layer of cylindrical cells with well marked inner boundaries and oval, deeply staining, peripherally placed nuclei.

Sudan IV revealed the presence of large amounts of lipid in the inner portions of the cells and in the lumina (Fig. 3).

A silver stain, employed to demonstrate the reticulum, showed that the latter surrounded the individual tubules with very little basket-weave arrangement between them (Fig. 4).

DISCUSSION.

The tumour is an encapsulated, luteinized and hormonally active adenoma of the ovary.

The nature of its hormonal activity as deduced from the clinical history before and after operation—unfortunately neither a uterine curettage nor any hormone assays were carried out as part of the preliminary investigation—appears to be oestrogenic.

The tumour is highly differentiated but along unusual lines, the tubular arrangement being not unlike that present in Pick's testicular adenoma of the ovary which, however, is a virilizing tumour.

Traut and Butterworth¹ describe and illustrate a tubular type of granulosa cell tumour and state that it is extremely rare.

Similar types have been described by Varangot² and Henderson.³ In Henderson's case there was vaginal bleeding and precocious development of sex characters in a girl aged 7 years.

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Chemotherapy in Obstetrics and Gynaecology

BY

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TEN years ago, sterilization of the blood by chemical means had come to be looked upon more and more as an unattainable ideal. Famous and futile procedures had been undertaken with this object but it had not been proven that any germicide was capable of killing bacteria in blood in a concentration attainable clinically. Then, at one step the ideal of *therapia sterilisans magna* advanced from the domain of medical mythology and became a concrete fact of daily practice. In 1935 was introduced to the world the first of the chemotherapeutic agents which, the world agrees now, constitutes the greatest therapeutic discovery in modern medicine—Prontosil. The story of its development is interesting. In 1908, Gelmo¹ synthesized para-amino-benzene sulphonamide. In 1909, Hörlein, Dressel and Kothe² prepared azo dyes with sulphonamide which "were distinguished by greater fastness for washing than those of sulphonamide-free products," a quality they attributed to the intimate union of the protein cells of the wool and the dye. The precise date of the synthesis of the basic form of Prontosil (2:4 diamino-azobenzene-4'-sulphonamide) is not clearly known, but in 1932 Mietzch and Klarer³ applied for a patent covering the original Prontosil (hydrochloride of 4'-sulphamido-2, 4 diamino-azobenzene) and several other sulphonamide-containing azo dyes.

Early in 1935, Domagk⁴ announced that "haemolytic streptococci of human origin were injected into 26 mice . . . later, half of

them received . . . a single dose of a dark red dye (Prontosil) which had been synthesized by Mietzch and Klarer (Hörlein⁵) and all survived . . . Of the remaining animals which served as untreated controls . . . the last was dead on the 4th day."

In France, Levaditi and Vaisman⁷ confirmed Domagk's experimental results with mice, using a similar compound synthesized by Girard, as they had been unable to obtain supplies of Prontosil from the Germans who had protected its manufacture by patent. Later that year, the Tréfouels, Nitti and Bovet^{8, 9} suggested that the effective azo-dyes were broken down at the azo linkage in the tissues of the treated host, and that the curative agent was para-amino-benzene sulphonamide, now known as sulphanilamide. In addition to the reports of animal experiments, there appeared about a dozen case reports in Germany^{9, 10, 11, 12, 13} on the use of the drug in human infections—both streptococcal and staphylococcal—unanimously favourable, but of little value as evidence since in most cases the recovery of the patients was entirely ascribed to the treatment; too little allowance was made for the tendency to spontaneous cure of these infections. The cases were not assorted with sufficient care either clinically or bacteriologically, but the reports did serve to arouse the greatest interest in England, and laboratory experiments and clinical trials were carried out by Colebrook and Kenny on patients suffering from haemolytic

streptococcal puerperal sepsis at Queen Charlotte's Maternity Hospital. In June 1936, Colebrook and Kenny⁶ described the results of these trials which "one can say without fear of contradiction or thought of disparagement of the observations made by the continental investigators" were to arouse the interest of the world upon the subject of bacterial chemotherapy¹⁴; 38 women with severe haemolytic streptococcal puerperal infections had been submitted to treatment and cautious conclusions, instructed by the fine judgment and long experience of the staff of the hospital, were drawn as to the curative effect of the new drug. "Subject to confirmation by further experience," they said, "the impression has been gained that in many of the more severe cases the drug has exerted a definitely beneficial effect . . . 3 patients in whom there was generalized peritonitis on admission (1 with a positive blood culture) have recovered." Confirmation was quick to come. In December 1936, the same workers¹⁵ reported their results with 64 women treated thus. Three only had died, a mortality-rate of 4.7 per cent. The death-rate for similar cases in the previous 5 years was 22 per cent.

The death-rate for cases with positive blood cultures (haemolytic streptococci) dropped from over 60 per cent to 25 per cent. None of the treated patients developed pelvic or metastatic abscesses. The average stay in hospital for the 61 Prontosil-treated patients who recovered was 18 days, while that of the 61 consecutive non-fatal cases immediately before the introduction of Prontosil was 31 days. A year later Colebrook and Purdie¹⁶ confirmed that one of the notable effects of sulphonamide therapy is the way in which it prevents a spread of the infective process from the placental site. In their series of 106 patients parametrial or extra-uterine spread occurred in only 5 per cent and in

these the spread was only of small extent. These authors also showed that, nevertheless, sulphonamides do not lead to a rapid destruction of the haemolytic streptococci, for the organisms can be recovered from the birth canal of treated patients weeks after clinical recovery has taken place, and that, therefore, operative procedures must still be avoided as far as possible or postponed until an effective blood concentration of sulphonamide has been reached, when the chance of an extension of the infection resulting from operative trauma will be greatly reduced.

The use of the drug Prontosil and its modern successors is now widespread, but it is interesting to note that Colebrook and Kenny's first results have never been bettered, and appear to represent the maximum that can be reached until the ideals of quick clinical and bacteriological diagnosis and early and adequate treatment can be made universal. It is also of interest that the dosage devised by these first workers on mainly clinical experience has become the standard for nearly all the sulphonamide derivatives and has been shown to give the necessary bactericidal concentration of the curative agent in the blood in most cases. Hard experience has shown that the more massive doses of the newer sulphonamides sometimes advised are unnecessary, distressing, and occasionally dangerous in their toxic effects.¹⁷ The intent is to reach a blood-concentration of the drug of 10 to 15 mg. per cent as quickly as possible¹⁷ and to maintain these levels until the patient has been afebrile for a few days. The 4-hourly dosage scheme is important since only thus can even concentrations be maintained in the blood.¹⁸ Occasionally, patients are encountered in whom the prescribed dose of sulphonamide does not give the desired concentration in the blood. In such individuals, clinically recognizable by their

unfavourable progress, the dose must be increased until the proper values are obtained. In the experience of many¹⁷ in all branches of medicine, unfavourable results with the drug have been more often attributable to this failure to achieve correct concentrations of the drug than to the rare presence of insensitive or resistant strains of streptococci. In these latter cases penicillin should be the immediate resort. It is very often customary, in these days, to give a large initial dose of the chosen sulphonamide in order quickly to establish effective levels of drug in the blood of patients stricken with severe infections—this dose being usually of 4 g.¹⁸ The reviewer hesitates to recommend this large dose in obstetric or gynaecological practice and prefers to build up the effective level over the first 24 hours, as was found possible by Colebrook and Kenny. In any method of administration adopted, an average of 1 g. of the drug per 10 kg. of body-weight per 24 hours is the standard dosage,²⁰ with, in women, a maximum daily dose of 6 g. during the febrile period and for 2 to 3 days after. Then the dose may be halved for 3 to 4 days and halved again for 3 to 4 days, making an average of 40 to 45 g. in all, in severe infections. Below is reproduced, for historical and topical interest, the original scheme of administration devised by Colebrook and Kenny.¹⁵ Each 20 c.cm. of the Prontosil given intramuscularly represents 0.5 g. With the modern sulphonamides parenteral therapy is necessary only when oral therapy is impossible. The blood of the patient, whose clinical record is here shown from the books of Queen Charlotte's Maternity Hospital, gave a growth of more than 5,000 colonies of haemolytic streptococci per c.cm. on culture in the first 2 days, and of more than 3,000 colonies on the 3rd day. It may be seen, therefore, that the drug and the scheme of dosage were submitted to a

very severe trial, and in view of the fact that such a large number of haemolytic streptococci are usually observed only in the terminal stages of a fatal infection, the patient's prompt recovery was astonishing but must have been imitated many thousands of times since 1936.¹⁴ The picture will, however, explain the reviewer's personal predilection for the original Red Prontosil in cases of desperate illness.²⁰

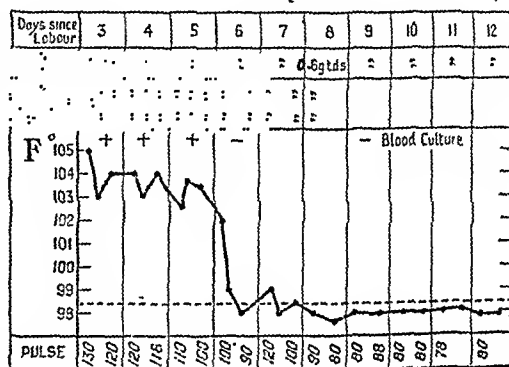


Chart showing a typical scheme of dosage in a case of puerperal septicæmia.

Despite the famous drop in the mortality from puerperal sepsis^{21, 22} the picture does not call for complacency. Colebrook,²³ in 1935, in the course of a plea for the use of effective antisepsis in midwifery, calculated that 6,000 to 7,000 women became infected with haemolytic streptococci in childbirth each year in England and Wales, and some 1,200 to 1,500 of these died. We know, from the falling death-rate, that the vast majority of these now recover under treatment with sulphonamides, but the incidence of this fearful disease shows no such happy decline but indeed a rise!^{21, 22} In 1934 there were 597,642 live births in England, with 8,431 cases of puerperal fever (14.1 per thousand) and 1,212 deaths (14.4 per cent). In 1939, 619,352 babies were born, 9,252 mothers were infected (14.9 per thousand), although only 476 died (5.2 per cent). These are the last figures we can analyse; they cover years of peace, before such considerations as increase in primi-

gravity, scattering of population and deterioration of medical services could be advanced to mitigate the sad facts. The same has occurred between the years 1936 and 1940 in the United States of America. In some centres, notably, from the reviewer's personal knowledge, at Queen Charlotte's Maternity Hospital and the Obstetric Unit of the British Postgraduate Medical School,²⁴ years may pass without the occurrence of a single case of haemolytic streptococcal infection in the puerperium—the sincere application of preventive measures having brought about the virtual eradication of sepsis. But the increasing figures of incidence of the disease for the whole country forces the belief that the introduction of the sulphonamides may not have been an unmixed blessing for childing women—that against the improvement of obstetric technique in some centres may be set a new recklessness in others, engendered, paradoxically, by confidence in the power of the sulphonamides to cover errors of judgment. The boast of the obstetrician should not be that since 1935 he has not had a single maternal *death* from sepsis, but that, with a realization of the serious consequences of the disease, he has reduced or banished the *incidence* on his service.

In 1937, Kenny²⁵ drew attention to one of the most evil of the remote effects of puerperal sepsis. In a group of 100 young women who had recovered spontaneously from the disease, during 4 to 5 years of the subsequent active childbearing period of life, there had been achieved only 5 pregnancies and only 4 live births. The average age of the patients at the time of this follow-up was 27 years—thus, it appeared that the ravages of the disease had definitely diminished the fertility of 95 young women aged 22 to 23. These distressful figures were confirmed almost exactly by Barr in 1939.²⁶

Cure, therefore, however certain and dramatic with the new chemotherapeutic agents, is not enough. Colebrook and Kenny⁶ were the first to advance the possibility that the prophylactic use of sulphonamides might control the development of puerperal infection in women who, either from the nature of the delivery or its environment, had undergone the risk of streptococcal contamination. Kenny²⁷ warned that small doses were ineffective for prophylaxis, and the earliest large-scale clinical experiment carried out by Johnstone²⁸ giving only 2 to 3 g. daily for the first week of the puerperium to all women delivered on his service in 1938, showed that these doses had no power to diminish the incidence of streptococcal infections, the results being in no way better than those of the control period, the previous year. It seems, therefore, in the present state of our knowledge, that prophylaxis can be achieved only by the attaining of "curative" levels of the drug in the blood by "curative" dosage. Recently, that this may be so has been demonstrated by Geisendorf and others²⁹ who gave full curative doses (large initial dose and maintenance doses for 1 week—31 g. in all) to all women delivered on a large service in Switzerland, for they found that postpartum urinary infections were reduced to one third of the incidence found in untreated controls, and that pelvic sepsis as manifested by thrombophlebitis also occurred one-third as frequently. Le Lorier,³⁰ quoted by Geisendorf and by Domagk,³¹ gave sulphanilamide prophylactically to 3,390 parturient women in 1 year, and not only achieved a decrease in the incidence of uterine sepsis, but also observed only 18 cases of urinary infection as compared with 76 such among the same number of untreated controls. The reviewer shares Colebrook's^{23a} opinion that the drug should be administered prophylactically in certain

cases in which delivery has been difficult, or when exposure to streptococcal infection at or near the time of delivery has been known or suspected to have occurred. Also, that bacteriological investigation of the birth canal must be carried out as soon as possible thereafter, especially in cases in which gross traumatism has been incurred, as the infecting organisms are then frequently the anaerobic streptococci against which the sulphonamides have not as yet been shown to prevail, and where the toxicity of the drugs may weight the balance against an already poor chance of recovery. The administration of the drugs to all women in labour is open to strong objection. "The flair of the accoucheur is reduced to the rôle of a distributor of pills."³⁰ The proportion of intolerants to the sulphonamides is not large, but if the number of cases treated increases, the problem of intolerance will become important; the price of the medicament is not negligible if employed in full doses in thousands of cases a year; the number of cases of sulphonamide-resistance would also increase.

Local Implantation of Sulphonamides.

Colebrook and Kenny in 1936⁶ showed that in mice a large subcutaneous implant of Prontosil in suspension formed a depot from which absorption of the drug and protection from experimental infection might continue for some weeks. Purdie and Fry³² in 1937 reported a case of chronic infection of the skin and subcutaneous tissues which had refused to heal for 3 years following puerperal sepsis, but healed completely within 6 weeks under local treatment with sulphanilamide powder. They pointed the way to the now widely used measure of using intraperitoneal deposits of the drug for both local and systemic antiseptic effect in the presence of known or suspected infection. Enormous concentration of the drug (200 to 1,000 mg. per 100 c cm.)

can be obtained at the site of implantation and maintained for many critical hours before gradually subsiding.¹⁷ The most valuable application of this manoeuvre in the obstetric field has been the habit of scattering 10 to 15 g. of the more soluble sulphonamides (sulphathiazole or sulphadiazine) over the uterine incision in Caesarean section in infected cases. In the reviewer's opinion, supported by those of many others¹⁷ this may enable the obstetrician not only to perform abdominal delivery with confidence in doubtful cases, but also to avoid the mutilation of the Porro operation, and to conserve the uterus even in infected cases. A seemly method is to place the drug in a finely powdered and sterilized³³ condition under the peritoneal flap of the bladder, which is then drawn up over the wound in the lower uterine segment and sutured at a higher level to complete the operation. Systemic therapy should not be begun for 2 days after implantation, and thus a possibly nauseated patient may be spared the oral intake of the drug. The intraperitoneal deposition of the drugs is also valuable in gynaecological operations in the presence of peritonitis¹⁷ or in cases in which soiling of the peritoneum cannot be avoided, and is useful also when the abdomen has been inadvertently opened in acute salpingitis.

Intrauterine deposition of sulphonamides has not been used to any known extent in this country although such tamponage has been suggested in both Latin and North America.^{34, 35} It is probable that absorption of the drug through the large uterine sinuses would be abrupt, and, in the case of the less soluble sulphonamides, possibly dangerous.

Urinary Tract Infections.

The last 10 years have seen as great a change in the diagnosis, management and treatment of infections of the urinary tract

as of puerperal sepsis. Fuller's¹⁶ discovery in 1933 that beta-oxybutyric acid produced by the ketogenic diet was a urinary anti-septic gave excellent results in ideal conditions, but the diet is so difficult to adhere to in the acidosed, nauseated, pregnant woman as to be impracticable. In 1935, Rosenheim¹⁷ introduced mandelic acid which, while simple to administer and very effective, is open to the same objection as it has a definite therapeutic effect only when the pH of the urine is 5.0 or lower, a figure usually impossible to attain in pregnancy or early puerperium. In 1937, Kenny, Johnston, von Haebler and Miles¹⁸ showed that sulphanilamide in small doses produces a rapid decline in clinical symptoms and bacterial infestation of the urinary tract in pyelitis of pregnancy and infections of the urinary tract encountered in obstetrics and gynaecology generally. Cuthbert,¹⁹ in 1938, reported good results with sulphonamides in urinary tract infections in the puerperium, whether or not these were complicated by genital sepsis. All these and other workers^{19, 20} had the best results when the infection was due to *Bact. coli*, in mixed infections the results were not so good. Penicillin combined with sulphonamide may well provide the remedy in these cases.²¹ It is important to judge each case considered suitable for chemotherapy not only by purely clinical evidence, but on microscopic examination of the urine and the bacteriology of the urinary tract. Jäämeri¹⁰ found that the urine of 600 pregnant or parturient women contained organisms of the colon-aerogenes group in 16.3 per cent of cases, and four-fifths of them had no clinical signs of the disease. Dodds⁴¹ showed that the *Bact. coli* can be demonstrated in the urine of 7.5 per cent of pregnant women, but that less than 1 per cent develop pyelitis. Douglas¹⁹ found a significant infestation of the urinary tract with *Bact. coli* in 15 per cent of

cases of puerperal fever. The predisposing hormonal factors associated with pregnancy, labour and the puerperium are obviously directly responsible for the development of conditions of the urinary tract of increased vascularity, dilatation, atony, hyperplasia and oedema, all combining to produce urinary stasis,⁴² apparently the primary inducing factor in the introduction of sepsis but possibly the reason, too, for the therapeutic concentration of the drug obtainable with small doses. Trauma during labour is an important factor in puerperal urinary infections as injury to the bladder, a very susceptible organ, is usually followed by infection. Also, neglect to observe atony of the bladder during the early puerperium which necessitates repeated or continuous catheterization constitutes another predisposing factor in the production of puerperal urinary tract infections and the sulphonamides should be administered prophylactically in such cases. [In gynaecological practice] with rare exceptions, we do not have to deal with these hormonal influences, but the proximity of the genital and urinary systems frequently leads to complications spreading from the one to the other. Relaxations of the anterior vaginal wall often cause residual urine in the bladder which is followed by infection, and in gynaecological surgery trauma to the urinary tract is very often inflicted.]

For all these infections specific treatment is now limited to the various sulphonamide drugs. Sulphanilamide is most widely used in this country because of its cheapness, availability and infrequent production of renal complications. Sulphapyridine should never be used in pregnancy because of its high toxicity. Sulphathiazole is effective against staphylococci as well as *Bact. coli*, but has the highest capacity for the production of crystalluria.¹⁹ We therefore do not recommend its use when renal com-

petence is in question. Douglas³⁸ writes highly of sulphadiazine, but his recommended dosage of all the sulpha drugs is unnecessarily high as are those advised by Browne³⁹ quoting the Medical Research Council War Memorandum.⁴⁰ Kenny and Johnston⁴¹ and Cuthbert⁴² showed that a satisfactory concentration of the drugs could be achieved in the urine of pregnant or puerperal women by the administration of 1.5 to 3 g. per day, and over and over again experienced observers^{43, 44, 45, 46, 47} have shown that 2 to 2.5 g. per 24 hours in adult patients is all that is needed. This dosage rarely needs to be exceeded except in fulminating pyaemia or pyonephrosis, the now very unusually seen developments of pyelitis. Usually, with these small doses, the causative organisms are eliminated within 4 days.⁴⁸ If a satisfactory therapeutic response is not obtained in a few days, further investigation of the urinary tract becomes necessary and pathological obstruction or anatomical abnormality will usually be found. One should never persist with therapy in the hope that prolongation of the period of treatment will accomplish cure. Failures or recurrences should be subjected to complete urological investigation.⁴⁹

There is not usually the necessity to add alkalis to the sulphonamide course although Helmholtz⁵⁰ and others⁵¹ consider this important. This is particularly true of sulphanilamide, which drug Kenny and Johnston⁴¹ showed to have a tendency to alkalize the urine. But Gilligan⁵² says that sulphadiazine and sulphathiazole are respectively 20 and 13 times more soluble in a urinary pH of 7 to 7.5 than of 5.0, also that the latter drug has a tendency to acidify urine. Therefore, if either of these drugs is used, sodium bicarbonate in adequate doses should be exhibited as well. Fluid intake (3,000 c.cm.) and urinary output (1,500 c.cm.) should be carefully

maintained and oliguria treated as a warning sign of crystalluria. It occurs usually with unnecessarily large or prolonged dosage.⁵³

The prophylactic administration of the drugs for 3 to 4 days before and after gynaecological operations is recommended for the prevention and control of urinary tract infections. Good convalescence is promoted especially if retention of urine occurs and necessitates catheterization. Waugh, McCall and Herrell⁵⁴ have shown that sulphonamides deposited intraperitoneally at operation are excreted in effective amounts from the urinary tract for many days and thus reduce materially postoperative morbidity due to urinary infection.

Venereal Disease.

The treatment of gonorrhoea by the sulphonamides has marked a milestone in the history of venereal disease. The reported results of the treatment in women are even more brilliant than those reported of males.^{55, 56, 57, 58, 59} There has been much discussion and dissension of opinion as to when the treatment should be begun for optimal results, and whether the patients should be hospitalized during treatment. The original rate of cure, 93.4 per cent. obtained in 1938 by Mahoney,⁶⁰ in a group of 61 women ill with chronic infections and hospitalized, has not been surpassed. Therefore, it has seemed good to many workers to delay treatment in the female patient as in the male, until a partial degree of immunity to the gonococcus has been developed. But the remote effects of the untreated spread of the disease in females can be so serious, or even dangerous (if subsequent pelvic surgery becomes necessary), that informed opinion now urges the treatment of the infection as soon as it is recognized in the early stages. This opinion has been fortified by the observations of

McElligott¹¹ and others^{14, 15, 16} that the treatment with sulphonamides of gonorrhoea in women almost entirely abolishes the spread of the disease, especially when combined with hospitalization so that conditions of treatment and rest can be controlled;¹⁷ and if extension to the adnexa does occur, rapid resolution can be expected with this therapy. Grodberg and Carey¹⁷ show that even when acute masses significant of salpingitis develop, these resolve with treatment in 10 to 14 days. This has been confirmed by others.¹⁶ As to dosage, the reviewer considers that the moderate amount of the drugs advised by Long,¹⁴ i.e. 4 to 5 g. daily for 3 days, followed by 2 to 3 g. daily for a week, is enough. Even smaller doses¹⁷ have given as good results and larger doses no better.¹⁶ A convenient and memorable scheme is that devised by Durel¹⁹ with sulphapyridine in the treatment of male gonorrhoea, 3 g. daily for 3 days, 2 g. daily for 3 days, and 1 g. daily for 3 days. The single massive dose of sulphonamides suggested by Pappas⁶⁰ in the treatment of the disease in males has also been tried in females by Strauss⁶¹ who finds that a single day's therapy with 8 g. of sulphathiazole or sulphadiazine cured 90 per cent of his chronically infected cases. Cohn and Grunstein⁵⁸ compared 2 schedules of chemotherapy in women with gonorrhoea, some 80 per cent of whom had adnexal involvement. In one group, 12 g. of sulphathiazole was given over 3 days and in the other, 21 g. over 7 days, with almost identical therapeutic effect. A blood level of 5 to 7 mg. per cent during the period of treatment seems to be sufficient.^{14, 19} We are not dealing with a deadly but with a mutilating infective process in gonococcal disease. Our aim is to limit its local virulence and prevent its spread. The relatively heroic doses required in septicaemia and other generalized infections are directed to life-saving.

Local treatment is not usually necessary in females when sulphonamides are used, and this makes the treatment most valuable in pregnancy. However, heat therapy by Elliott's apparatus or diathermy is useful in chronic disease.¹⁶ It is a wise practice to give a course of a sulphonamide shortly before and after an infected pregnant woman is delivered, even if there has been apparent cure previously, both to protect the mother from the now rarely seen puerperal spread of the disease and to lower the virulence of possibly still-existent organisms in the birth canal in the interests of the baby. There is yet much information that must be gathered on the incidence of permanently damaged Fallopian tubes in treated cases of salpingitis. A recent paper by Barrows,⁵⁶ confirmed by Hunt and others,¹⁷ claims that in treated cases of gonococcal salpingitis the pelvic masses disappear in 80 per cent as compared with a resolution-rate of 20 per cent in untreated controls. Even severe cases have a 60 per cent chance of success, but late cases have poor results. There is however no note on the patency of the tubes thereafter. All^{17, 56} advise that even old-standing cases should have treatment with sulphonamides as some tubal salvage may result, the period of illness is shortened and eventual surgical treatment made safer and easier.

Pronouncement of cure in the infected female has not been made easier by the new chemotherapy, for so greatly has the sulphonamide group of drugs changed the state of affairs that it has become very important to classify separately tests for cure in those who have and those who have not had sulphonamides. Jones⁶² maintains that the sulphonamides "change the characteristics of the gonococcal slide," the changes consisting in marked alterations in the morphology and staining reactions of the gonococcus. Great care must be exercised therefore to prevent the asymp-

tomatic carrier being loosed upon the public. Pelouze⁶³ insists that re-examination should be made on several occasions after apparent cure, preferably after or during a menstrual period and after resumption of sexual life (in which the partner should be protected by a condom) for some months. He also claims that it is possible for a treated patient to transmit asymptomatic disease, the victims being unaware that they are infected until they transmit the disease to another. The incidence of sulphonamide-resistant cases is probably low in properly treated cases and it is likely that some of them are due to reinfection. Penicillin, when available, seems to be of use here.⁷¹

Vulvovaginitis in Infants and Children.

After several early favourable reports upon the use of sulphonamides in this condition (Brown,⁶⁴ Hoffmann,⁶⁵ Gaté and co-workers⁶⁶), there have recently been publications showing that their scope is limited and the results disappointing. Brown emphatically declared her results to be brilliant, yet Hoffmann claimed but 16 cures among 25 young girls and found that only 2 of the remaining 9 were cured by further courses of the drug. Gaté and Cuilleret claimed 100 per cent cure in 8 affected infants. Alyea⁶⁷ reported only a 20 per cent permanent cure-rate and Grodberg,⁶⁷ Compton¹⁴ and Long¹⁴ were also discouraging. Sandes⁶⁸ has found that little girls between the ages of 2 and 10 years develop toxic symptoms readily and do not tolerate the drug well. Her paper and those of the others all deal with the use of the earlier sulphonamides and it may be that the later preparations will be at least better tolerated by small children. The results in general remain far inferior to those obtained by the administration of the oestrogens.⁶⁹ In a small number of cases of vulvovaginitis in young children in whom

the infecting organism is the *streptococcus haemolyticus* and *staphylococcus aureus* the reviewer has obtained rapid and permanent cure with a combination of oestrogen and sulphanilamide.

A recent paper by Cohn, Steer and Adler⁷⁰ has claimed a very high rate of cure with sulphapyridine in anorectal gonococcal infection in young children.

With the increasing availability of penicillin for civilian use and its already known value in the treatment of sulphonamide-resistant cases of adult gonorrhoea,⁷¹ it may be hoped that a treatment will be evolved for these sad infants wherein local therapy and examinations may be kept to the minimum consistent with the required knowledge of the progress of a case.

Ophthalmia Neonatorum.

The annual returns from the Ministry of Health⁷² show that for the 7 years, 1934 to 1940, 44 children in England and Wales were blinded from ophthalmia neonatorum; during 1941 and 1942, only 1 case was reported. The incidence of impaired vision from this disease likewise has declined, the figures for the two periods being 190 and 14 respectively. In 1931, blindness from ophthalmia constituted 21 per cent of all cases of blindness in children admitted to schools for the blind managed by the London County Council, in 1943, the proportion was 9.8 per cent.⁷² In the United States of America, in 1941, the proportion was 5.6 per cent compared with 28 per cent earlier.⁷³ Authors in both countries^{72, 73} stress that while silver nitrate is still the best preventive measure, it has very definite limitations, and the improvement in the figures they quote is largely due to the sulphonamides "in which we have a therapeutic agent that makes blindness or impaired vision from this affection no longer tolerable."⁷² Treatment should be both prenatal—diagnosis and treatment

of infections in the prospective mother, and postnatal use of a prophylactic agent in the eyes of the newborn infant and vigorous use of the sulphonamides in declared disease. The drug of choice is now sulphathiazole in doses of 1 gr. per pound of body-weight, given orally.⁷³ Cases resistant to sulphonamides should receive penicillin therapy^{72a, 74, 75} and there still seems to be a place for artificial fever therapy should chemotherapy fail.

Choice of Drug, Toxicity, etc.

At the present time we have available for general use in this country, adequate supplies of sulphanilamide, sulphapyridine, sulphadiazine, sulphamezathine and sulphathiazole, and limited amounts of others such as sulphamerazine and sulphacetamide.

The drug of choice is that with the greatest specific bactericidal effect and least toxicity. All the sulphonamides are toxic, the poisonous effects are commonly believed to be due to sensitivity or idiosyncrasy—neither the quantity of the sulphonamide used nor its level in the blood seems to be definitive in producing fatal lesions although in general large and especially prolonged doses are dangerous.^{76, 77} The dangerous complications of sulphonamide therapy are those affecting the haemopoietic system and causing agranulocytosis and haemolytic anaemia; and the urinary tract by mechanical damage leading to anuria and uraemia. This last is effected by the deposition of calculi composed of crystals of the drugs in the renal tubules or pelvis.⁷⁸ Fatal doses have ranged from 96 g. to 0.6 g. in the production of agranulocytosis and renal injury respectively.⁷⁶ Agranulocytosis usually appears after 2 weeks of treatment. The minor complications such as met- and sulph-haemoglobinaemia producing the now well-known lividity of the skin des-

cribed by the early workers⁶ are never serious; development of drug fever or rashes is usually an indication of a degree of intolerance, but there is no definite evidence to suggest that these reactions are precursors of the more serious ones.⁷⁹ Drug fever and drug rash usually appear after 9 to 12 days of treatment, and are considered to be a sensitivity reaction and may be related to previous administration of the drug.⁸⁰ Drug fever may be high with rigors and should be suspected when improvement produced by sulphonamide is followed by recurrence of temperature while sulphonamide is still being given.⁷⁷

Recent reviews of deaths from the sulphonamides⁷⁹ show that all the popular preparations are incriminated, sulphanilamide being still apparently the least dangerous next to sulphadiazine, but comparing poorly with the latter drug in its range of bactericidal action. Sulphathiazole, while effective in a wide field of diseases and well tolerated by pregnant women, has the highest incidence of renal complications and can cause agranulocytosis. It is also prone to produce drug-sensitivity and should not be used again if subsequent therapy is needed. Sulphapyridine is widely effective but most toxic for all systems, and should not be used in pregnancy or the puerperium. Sulphadiazine is both effective and of low toxicity; it has not as yet appeared in the literature of agranulocytosis but has caused fatal uraemia. It appears to be effective in quite low concentrations in the blood (3.5 to 5 mg. per 100 c.cm.¹⁹) so that a dosage of 4 to 5 g. per 24 hours may be used with success. Sulphamerazine is as bactericidal as sulphadiazine, more soluble and more rapidly absorbed, so that even smaller doses give a constant therapeutic level in the blood. Its toxicity is about the same.

Sulphamezathine, a recent British* production, is less toxic than sulphapyridine,^{79a}

is rapidly absorbed and being freely soluble the risks of urinary complications are minimal.^{79b} Agranulocytosis or the disturbance of erythropoiesis has not been observed even in cases where the blood-concentration of sulphamezathine has reached 30 mg. per cent.^{79a} Its use is therefore recommended in pregnancy or in cases where renal efficiency is doubtful. It appears, however, from the latest available evidence that sulphamezathine gives only variable clinical results in gonorrhoea.^{79c}

The toxic effects of all these drugs on the haemopoietic system may be controlled by a watch on the blood picture if there is a necessity for a long course of treatment, appropriate measures of stimulation and replacement being taken if signs of damage appear, and the drug discontinued. It is important to remember that the clinical manifestations of blood dyscrasias from these drugs are faint in the early tractable stages; when they are marked, it is usually too late for effective remedy, and that, therefore, repeated blood-counts must be carried out after the first week or 10 days of treatment and before a second course of the drugs. Mechanical damage to the renal tract by crystalluria can be prevented by avoiding initial massive doses of the drugs, especially of sulphapyridine and sulphathiazole, encouraging a daily fluid intake of at least 3 pints during therapy and watching for signs of oliguria. Personal opinion reinforced by that of others^{80, 80} suggests that if there is a necessity to continue the administration of a sulphonamide despite the appearance of toxic complications or if a second or subsequent course becomes necessary in the treatment of a patient who has shown signs of intolerance in the initial course, another sulphonamide should be chosen; for example, if sulphapyridine be poorly tolerated, treatment may be continued or resumed with sulphamezathine or sulphadiazine or sulphaceta-

midate, this last drug especially in recurrent pyelitis of pregnancy.⁸⁰ In any review of the respective toxicity of the sulphonamides, it must be recalled that the smaller incidence of toxic effects claimed for any of the newer drugs may be due not only to lower toxicity, but in part to the fact that these have not yet been as widely used as the older preparations, and full reports of their application are not yet to hand.

PENICILLIN.

The chemotherapy of bacterial infections passed, as we have noted, from an ideal to reality with the advent in 1935 of Prontosil. During the rapid development of sulphonamide treatment which followed, other organisms than haemolytic streptococci were found to be vulnerable and it seemed likely that with the discovery of new drugs of this type all bacterial infections could be vanquished. But it was soon found that the sulphonamides had their limitations; even among the susceptible bacteria some strains are exceptionally resistant to the sulphonamide drugs and many species are wholly resistant. The time was ripe for a great new chemotherapeutic discovery which would provide a remedy where sulphonamides fail, and this was made by Fleming, the discoverer of Penicillin. Penicillin was discovered in 1929^{81, 82, 83} and used by its discoverer for differential culture, but, like Prontosil, its use for practical therapeutics was completely neglected until the Oxford workers started their investigation in 1938. It is now known to combine enormous antiseptic power with such a degree of freedom from toxicity in the human body that much more than a therapeutic concentration can be achieved in the blood without ill effect. Penicillin has fulfilled the hopes entertained with the sulphonamide drugs—deadliness to bacteria and harmlessness to the body to an

extent undreamed of by the most sanguine chemotherapist. All of our present knowledge of its clinical possibilities is based on the studies of Florey, his wife, and his colleagues.⁵⁴ Penicillin salts are used therapeutically, the sodium salt for systemic treatment and the more stable calcium salt for local application. Potency is expressed in Oxford units, an arbitrary amount devised by Florey by comparison with a standard preparation. The only penicillin-resistant organisms that interest the obstetrician and gynaecologist are the tubercle bacilli, and almost all the gram-negative bacilli including the typhoid-dysentery group, the *genus Brucella* and the frequent wound and urinary tract invaders, *Proteus* and *Ps. pyocyanea*.⁵⁵

Penicillin can be used by local application in suitable cases or by parenteral injection. It cannot be given by the alimentary tract as too much of it is destroyed by acid in the stomach or by bacteria in rectal infusion. Unfortunately, in view of its cost and scarcity, it is very rapidly excreted in the urine, so that to keep up a therapeutic level it is necessary to use continuous intravenous or 3-hourly intramuscular injection day and night, the daily dose for an adult being 120,000 Oxford units, in serious disease continued for 7 days or longer. The sudden and dramatic improvement often noted with the sulphonamide drugs is rarely seen; sustained and arduous treatment is the price of success.⁵⁵

In the present circumstances penicillin should be used systemically only in conditions intractable by the sulphonamides or when sulphonamide sensitivity, resistance or intolerance has been demonstrated clinically. Until recently, supplies of penicillin were not available in this country for general civilian use since the armed forces were justly receiving the bulk of the supply. Its use here is still restricted to cases of grave illness so that the few papers on its

use in obstetrical or gynaecological disorders and venereal disease have appeared mainly in the North American Press.

Puerperal Sepsis.

Keefer⁵⁶ reported 8 cases of post-abortal and puerperal sepsis treated with penicillin. Five of these were postabortal anaerobic streptococcal infections, 3 got better and 2 died. The 2 deaths occurred in women with septicaemia; the 3 recovered patients had negative blood cultures. The puerperal cases had localized uterine infections with haemolytic streptococci or staphylococci, and recovered. The effect of penicillin, therefore was not apparent in this series of cases. However, Mitchell and Kaumeister⁵⁷ gave 40,000 Oxford units of penicillin daily to a moribund patient with puerperal sepsis due to haemolytic streptococci, sulphonamide-resistant, blood culture positive, pelvic thrombophlebitis present. The woman recovered. The hopes of obstetricians have been raised by reports of the sensitivity of anaerobic streptococci to penicillin *in vitro*. I am indebted to Dr. Robert Cruickshank⁵⁸ of the L.C.C. Group Laboratory at Hampstead for the following account of his experience of penicillin and the sulphonamides in anaerobic streptococcal puerperal infections, and Mr. James Wyatt, Consultant to the puerperal fever unit at the North-western Fever Hospital, who confirms the clinical impressions in the letter: "We have tested half-a-dozen or more of the 'septicaemic' variety of anaerobic streptococci against penicillin and all have been highly sensitive *in vitro*. Unfortunately we had no luck with penicillin therapy—4 cases treated and 4 deaths—although in 1 at least the primary septic thrombophlebitis seemed to have cleared up at autopsy, in my experience a most unusual finding. We have treated 20 more

of the typical anaerobic streptococcal septicaemic cases with sulphonamides without any response, the fatality-rate was around 80 per cent. Of course, a number of these infections were 'mixed' with *B. necrophorus* or were pure necrophorus infections, and the 3 strains of this organism I have tested for penicillin have all been resistant. . . ." It is known^{23a} that bruised, lacerated, ischaemic tissues favour the growth of anaerobes. So that, thus far in chemotherapy, we have found no escape from the knowledge that good midwifery, the avoidance of undue traumatism of the birth canal, is our only present means of preventing the dangerous development of this disease.

Venereal Disease.

A small number of reports on the treatment with penicillin of venereal disease in women have appeared in the American press and are uniformly encouraging. Herrell and fellows²⁴ state that the drug is most useful in the treatment of sulphonamide-resistant cases of gonorrhoea; Cook²⁵ claims results far surpassing those obtained with the sulphonamides in the initial treatment of gonorrhoea in women. Greenblatt²⁶ suggests that the problems of the asymptomatic carrier and the possible development of penicillin-resistant strains of gonococci may be answered by using larger than apparently necessary doses of penicillin in treatment. He and his co-workers consider that, although cure may be obtained with as little as 60,000 Oxford units, doses such as 150,000 units should be used. Thompson²⁷ finds that, with this larger dosage, 98 per cent of cases are cured and that it is quite free from toxic effect. The possibility that a coexistent early syphilitic lesion may be masked by treatment aimed at gonorrhoea has been raised.^{28a} It seems advisable to test the Wassermann

reaction of all penicillin-treated cases some 3 months later.

Penicillin has also been used by Lentz and his fellows²⁹ in the treatment of 14 pregnant women with early syphilis and 9 infants with congenital syphilis. They used total doses of 1,200,000 to 2,400,000 Oxford units, given by intramuscular drip in 8 days, and found that this was well tolerated by pregnant women. They think that the higher dosage is desirable. Although the period of observation has not been long enough to be certain that either mothers or babies have been cured, they state that miscarriage, stillbirth, and neonatal death are averted, the infants are born apparently healthy, and the course of the disease profoundly and favourably affected. The infected infants responded well to doses of 18,000 units per pound of body-weight, but grossly affected babies must be treated with smaller doses under careful paediatric supervision. A more recent paper by Lentz's colleagues, Platen and others³⁰ concerning 69 infants with manifest early congenital syphilis treated with 16,000 to 32,000 units per pound of weight shows somewhat unsatisfactory results, and the authors suggest that larger doses still, such as 40,000 units per pound, may give the optimal effect. In general, however, the immediate response of early congenital syphilis to penicillin, and its lack of toxic effect, has been gratifying; cutaneous and mucous lesions heal very rapidly and dark-field positive lesions become negative in 24 hours after the start of the treatment. Rhinitis is more lingering, but X-ray evidence of osteitis disappears in about the same time as with the metal salts. I feel that when treatment is being instituted primarily in the interests of the unborn child—the maternal syphilitic state being secondary, as in early infection in late pregnancy—penicillin should be chosen for its rapid beneficial effect, however imper-

maient, and its freedom from ill-effect. In a single case in my care, treated with large doses of penicillin, a woman in late pregnancy with a syphilitic rash and severe vulval sepsis, after a week's treatment both the rash and the vulval lesions disappeared entirely. The Wassermann reaction remains positive but this is to be expected during some weeks to come. She is as yet undelivered.

Ophthalmia Neonatorum.

Penicillin is now also being used in the treatment of ophthalmia neonatorum. Sievers⁷¹ reports that 8 patients were treated with intramuscular injections in total dosage varying from 60,000 to 330,000 units. Six of the 8 responded promptly with pronounced clinical improvement within 24 hours and complete recovery in 3 to 6 days. The specific organisms disappeared in smears and cultures in 9 to 24 hours after beginning the treatment. These results are equal to those obtained with sulphonamides and it may be that penicillin should be chosen for use in very ill or premature babies afflicted thus, because of its slight toxicity.

Sorsby,^{72a} too, claims that the dramatic results obtained by the use of the sulphonamides are paralleled by those given by penicillin. He has published results in a total of 47 cases of ophthalmia neonatorum treated by the local application of penicillin in the form of drops. He obtained optimum results with a concentration of 2,500 Oxford units per c.cm. in cases where the disease was caused by a whole range of organisms, gonococci, staphylococci and even the virus of inclusion blenorhoea. The drug is well tolerated by the infant's eye, irrigation is generally not necessary after 6 hours, clinical recovery sometimes takes place in a few hours.

In the Obstetric Unit of the British Post-

graduate Medical School penicillin eye-drops in 1,000 Oxford units per cent concentration are now being used routinely as a prophylactic measure in the newborn in place of silver nitrate. One drop is instilled immediately after cleansing the eyes and 1 drop an hour later after the bath.

Breast Abscess.

Since this complication of the period of lactation is usually due to infection with staphylococci, penicillin should be used as soon as possible to avert the need for surgery, and in combination with surgery when it is unavoidable. Private communications from London hospitals report its present use with oestrogens in mastitis, with favourable results in preventing the development of breast abscess. Fraser⁹¹ reports on the use of penicillin locally, combined with simple aspiration of breast abscesses or with surgical drainage. He thinks that healing is much more rapid than usual in the treated cases and the organisms quickly disappear. Suppression of lactation by stilboestrol was necessary in his cases to achieve the best results.

In the reviewer's small experience with staphylococcal infections affecting mother or child in the early days of the puerperium, there has occurred very rapid healing of localized lesions of the infants' scalps after injection under the surrounding skin of small doses of penicillin; and in a single case of staphylococcal osteomyelitis of the humerus in a 3-days-old baby, there was immediate favourable response with penicillin after extensive spread intractable to surgery and sulphadiazine.

Thus far, then, the wide bactericidal range and freedom from toxicity of penicillin make it the drug of choice in nearly all of the infections encountered in the field of obstetrics and gynaecology; and our

hope remains that newer chemotherapeutic discoveries will set still wider bounds to the victory over disease, or, better, that a general improvement in obstetric practice may soon reduce the number of cases requiring the use of penicillin, or the sulphonamides, or other curious measures.

" 'Tis not enough that through the cloud thou break,
To dry the rain on my storm-beaten face,
For no man well of such a salve can speak,
That heals the wound, and cures not the
disgrace . . . " ⁹³

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BOOK REVIEWS

"Principles and Practice for Pupil Midwives, Teacher Midwives and Obstetric Dressers." By R. CHRISTIE BROWN, M.B., M.S., F.R.C.S., F.R.C.O.G., and BARTON GILBERT, B.Sc., M.D., F.R.C.S., M.R.C.O.G. Infants' Section by RICHARD H. DOBBS, M.D., M.R.C.P. 2nd edition, 831 pages. London: Edward Arnold & Co., 1945. 15s.

This book is intended primarily as a textbook for the pupil-midwife studying for the examinations of the Central Midwives Board. The majority of pupil-midwives are already state registered nurses. The nurse who desires to become a midwife has to undergo some mental readjustment. Her training as a nurse has conditioned her to carrying out the doctor's instructions. Prepared only for delegated responsibility, she finds herself confronted, for the first time, with possible full personal responsibility. In most cases, it is true, she will be able to call in a doctor if required. But she must know when it is advisable to do so. For the first time she must learn to examine a patient for herself, to make a diagnosis, to rely on her own judgment and, perhaps, to carry out treatment in a grave emergency when a doctor is not available. She has not the medical student's scientific background to her training and her powers of reasoning have not been as well developed.

In this book the authors have made an effort to overcome these difficulties. The first 124 pages are devoted to a discussion of scientific principles, general anatomy and physiology. Matter and its structure, diffusion and osmosis, the elements of chemistry, energy, chemical changes in the body and the structure of the animal cell are discussed simply and lucidly. Throughout this section and also that devoted to general anatomy and physiology (in fact this is so throughout the book) care is taken to ensure that the reader will understand the subject matter. All that is discussed in this early part has a practical application to the actual obstetric facts which are recorded later. Careful

study of these opening chapters will lay a solid foundation on which the pupil can build understood facts—facts which will be remembered because they are understood.

The customary obstetric field is covered. A good balance is maintained between the more detailed description of normal childbirth, its physiology and management, and the complications with which the midwife may be faced while alone (e.g. postpartum haemorrhage, eclampsia, etc.) on the one hand and those fields which necessarily belong to the practitioner or obstetrician on the other, but about which the midwife must have some knowledge. There is also a satisfactory balance between dogmatic teaching and the reasonable discussion of conflicting views and theories on controversial matters. While it is difficult to single out particularly good chapters, antenatal care, normal labour, postpartum haemorrhage, the toxæmias, contracted pelvis and disproportion are, perhaps, worthy of special mention.

Exception can be taken to some of the authors' statements. We are told, with regard to toxæmia, that "in milder cases in which a faint trace of albumin alone is present, confinement to bed is not so necessary, the return of the patient to the doctor or clinic *once a week* (italics mine) will suffice. . . ." Plugging of the vagina by a midwife in abortion (p. 390) and central placenta prævia (p. 411) is likely to do more harm than good—even in exceptional circumstances. There is a tendency to over-emphasize the fact that it is inadvisable to hurry the birth of the after-coming head in breech delivery. The lack of prompt delivery at the right moment can be equally fatal with too rapid delivery. No mention is made of the Burns' technique. In Figs. 173 and 174a showing delivery of the after-coming head the attendant's hands are depicted in exactly the opposite rôle of that ascribed to them in the text. This makes the description difficult for a beginner to follow. It is unfortunate that the Lancefield

Group A haemolytic streptococci should be called Type A. The inexperienced reader may thereby become confused between the Lancefield Groups and the Griffiths Types.

Errors appear here and there. Recent work on the foetal circulation by "Berkeley and his colleagues" presumably refers to that of A. E. Barclay *et al.* Sir James Young Simpson is erroneously stated to have been Professor of Obstetrics in the University of Glasgow. Edinburgh has its Simpson Memorial Hospital as a tribute to its great professor. Happier wording might have been chosen to describe the positive signs of pregnancy (p. 311). The *ability* to hear the foetal heart beating or to feel foetal parts is surely not a positive sign of pregnancy.

There is an excellent section of 6 chapters devoted to the child.

This second edition of an already popular book can be recommended with confidence to the pupil midwife. In spite of being comprehensive it is of a good handy size—one likely to appeal to the average pupil who is apt to be frightened by too large a book. It may also be read with genuine profit by those whose lot it is to teach the pupil-midwife.

ANTHONY W. PURDIE.

"Endocrinology of Women." By E. C. HAMBLÉN, B.S., M.D., F.A.C.S. Clinical Professor of Endocrinology and Associate Professor of Obstetrics and Gynaecology, Duke University School of Medicine, Durham, N. Carolina. 571 pages with 157 illustrations. Price 8 dollars. Springfield, Illinois: Charles C. Thomas. London: Baillière, Tindall and Cox. 1945.

This is one of the most valuable and outstanding contributions to the literature of endocrine disorders in women.

It is not intended as a second edition to Professor Hamblén's book "Endocrine Gynaecology," written 5 years ago, but represents an up-to-date summary and critical survey of clinical *data* and experimental work. The arrangement of the various subjects in 5 subdivisions affords easy reading and makes it a practical reference book. Two kinds of references are used, footnotes for documentation and a list of references at the end of each chapter for supplementary reading.

It is pleasing to see a book which does not contain a variety of unspecific and confusing terms for menstrual disorders and which does not list absence of or abnormal uterine bleeding as disease.

Symptomatic therapy is strongly opposed and the outlined treatment is accordingly aimed not at the correction of the menstrual disorder but at the underlying cause.

Many readers accustomed to the present-day nomenclature of menstrual disorders and their treatment as disease entities according to fixed schedule will at first move on unsure ground. However, the excellent presentation of the material and logical approach to endocrinology facilitates the understanding of the subjects described.

In the treatment of functional disorders Hamblén adheres, on the whole closely, to the physiology of the endocrine glands. Androgenic treatment in women is strictly opposed on the grounds of its unphysiologic nature.

The same view is outlined for the use of oestrogens in the climacteric; whenever its administration becomes necessary for symptomatic relief, the author advocates only small doses over 20 days and a 10-day rest period.

It is surprising to see that despite his fundamentally sound and critical approach to endocrinology, Professor Hamblén recommends fixed treatment schedules for hypo-oestrogenism and abnormal uterine bleeding.

In the treatment of hypo-oestrogenism Professor Hamblén ascribes to oestrogen withdrawal bleeding only nuisance value and advocates doses not high enough to cause bleeding. No value is placed on the psychological effect of regular "menses."

Part I is a short but detailed discussion of all endocrine glands, including the testes. The description of each gland is preceded by a history of discoveries concerning it. The secretory control, functions and interrelation of the glands, the chemistry and action of hormones are very well described.

The 2nd section deals with the applied endocrine physiology of the foetus, the infant, the child, and adolescent, and of conception; of the menstrual, anovulatory, gestational cycle and of the climacteric.

The 3rd part is devoted to endocrine diagnostic methods and gives a survey of the main procedures, including endometrial biopsies, vaginal smears,

chemistry of the blood and urine, and denotes the particular value of each.

Functional disorders of the various endocrine glands, their treatment and rôle in gynaecology are discussed in the 4th section.

The last part deals with endocrinology applied to gynaecological diseases. There is detailed dis-

cussion of abnormal uterine bleeding, complications of pregnancy and the climacteric.

The diagnosis and treatment of both husband and wife in sterility are well described.

There are numerous very good illustrations and diagrams attractively arranged throughout the book.

REVIEW OF HOSPITAL REPORT

THE ROTUNDA HOSPITAL, DUBLIN.

Founded 1745.

Incorporated by Royal Charter 1756.

BICENTENARY CONGRESS, JULY 1947.

THE recent victory in Europe encourages the hope that the Congress of Obstetrics and Gynaecology that is to be held in Dublin in the second week of July 1947, in connexion with the Bicentenary of the Rotunda Hospital, may be of a representative and international character. Already various speakers from Great Britain, America and Europe

are being invited to open discussions on various subjects and a certain amount of preliminary work is at present being done.

The subjects chosen for discussion include: Eclampsia, Shock in Obstetrics, Foetal Mortality, Puerperal Sepsis, the Modern Approach to the Problem of Sterility, and an Historical Review of the progress in Midwifery during the past 200 years.

These various subjects should promote a series of interesting discussions, and, from the scientific as well as from the social standpoint, there can be little doubt but that the Rotunda Congress will be a most valuable and enjoyable addition to the resumption of international medical relations.

Obituary

Carlton Oldfield

(1871—1945)

CARLTON OLDFIELD came into gynaecology at a time when the horizon of that subject was being enlarged. No longer was the physician-accoucheur, as he was often called, to be restricted to attendance at childbirth and the repair of damage caused at that time; the abdominal surgery of the uterus and appendages was coming into his purview and Oldfield made himself a master of this in a city where new surgical ground was being broken almost every day.

The Goodenough Report on medical education has recently stressed the value of experience in general practice to the specialist in training. Carlton Oldfield had the advantage of a long period in general practice before he specialized.

In the early years of this century the ambitious gynaecologist often took the higher qualification not only in surgery but also in medicine. Oldfield became first a member of the Royal College of Physicians, and later, 16 years after he qualified, a fellow of the Royal College of Surgeons. The work for these examinations was all done in time he managed to find while fully employed in a very busy general practice. I remember one of his friends telling me many years ago how he would work late into the night in front of the fire with a book on the mantelpiece, standing to keep himself awake.

His early training after qualification was done under one of the greatest of Leeds surgeons, Mayo Robson. He was appointed

surgeon to what is now the Hospital for Women, and on Dr. Hellier's retirement he succeeded him as gynaecological surgeon to the Infirmary at the end of the first world war. Later he succeeded Dr. Croft as Professor of Obstetrics and Gynaecology in the University of Leeds. He retired from these two posts under the age limit in 1930.

He was a great teacher, and always brimful and overflowing with fresh ideas. When he came in to operate he would suggest problems for investigation as he walked up to the theatre. He was a fine surgeon, equally skilled in the abdominal and vaginal work of his speciality. I remember hearing a well-known Yorkshire surgeon say that Oldfield was the best gynaecologist he had ever seen operate. I unfortunately never saw very much of his work in obstetrics, but in gynaecology his clinical acumen and judgment were outstanding. He lost a little finger in the middle of his career, but this in no way interfered with his manual dexterity and skill. Those who have heard him will readily recall his teaching, speaking in a very quiet voice, with characteristic gestures of the hands. Like all good teachers, he recognized the value of constant repetition. He took up new things with enthusiasm. When, rather belatedly, the British Schools took up treatment by radium in the late twenties, he at once made the new subject one of his chief interests. His best known contributions to medical



CARLTON OLDFIELD

literature were perhaps that on the pernicious vomiting of pregnancy, in the approach to which he was one of the first and one of the most persistent to stress the psychological element, and that on puerperal general peritonitis, in which he was a firm advocate of the benefits of drainage. He was recognized as an exceptionally skilful obstetrician, and so was fittingly chosen to revise the last two editions of that obstetric classic, Herman's "Difficult Labour."

He had many interests outside medicine, notably hunting, farming and golf. In connexion with golf one may allude to his friendship with Lord Moynihan. Donald

Bateman—in Moynihan's *Life*—tells of an occasion on which the two were accompanied on their round by a fellow doctor, who remarked that they did a good deal of talking. Moynihan replied "Oh, yes, you mustn't think that we come here just to play golf. We settle the affairs of the universe while we are playing!"

Our sympathy goes out to Mrs. Oldfield and her children in their great loss, and we mourn the passing of a distinguished son of the Leeds School.

ANDREW M. CLAYE.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

A Meeting of the Council was held on Saturday, May 26th, 1945, in the College House, with the President, Mr. Eardley Holland in the Chair.

The following were formally admitted to the Fellowship by the President:

Caroline Ann Elliott.
Eric Arthur Gerrard.
Robert James Kellar.

Meave Kenny.
Frederick Ross Stansfield.

in absentia:

Geoffrey Shedden Adam.
Arthur Machen Hill.
John Joseph Kearney.
William Keverall McIntyre.

Bruce Toomba Mayes.
Herbert Kenneth Pacey.
Frank Stabler.
Geoffrey Ashburton Thompson.

The following were formally admitted to the Membership by the President:

Amelia Esther Burch.
Eric Garland Collins.
Jadwiga Karnicki.
Gladys Elizabeth Keith.

Dorothea Mary Kerslake.
Dorothy Margaret Shotton.
Benjamin Gibson Gunlys Spiers.

in absentia:

James Paton Orr Erskine.
Andrew Bertram Hay.

Sybil Grace Mocatta.
Dorothy Joan Thompson.

The Annual General Meeting of the College was held on Saturday, May 26th, 1945, in the College House, with the President, Mr. Eardley Holland, in the Chair.

The following were elected to Council in place of those retiring by statutory rotation:

Representative of the Fellows:
Malcolm Donaldson.

Representative of the Members:
Donald Blake Fraser.

The following were re-elected to the Council:

Representatives of the Fellows:

A. M. Claye.

C. A. G. Macafee.

H. J. Malkin.

Representative of the Members:

Hector Ross MacLennan.

INDEX TO CURRENT LITERATURE

In this Index an endeavour will be made, so far as war conditions permit, to maintain an up-to-date record of all titles bearing on obstetrics and gynaecology and the infant. The classification aims at making immediately available for the reader the titles under the various subject headings. In the majority of instances the title is obtained from the original publication. Where this has been impossible, the title has been obtained from the abstracting journal shown in brackets. Reprints will be welcomed and should be sent to the Editor.

Any inquiries should be addressed to Miss D. F. Atkins, British Post-graduate Medical School, Ducane Road, London, W.12.

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ANATOMY

1. "Study of Bantu female pelvis." O. S. Heyns. *Journ. Anat.*, 1944, LXXVIII, 151-66. (*Brit. Abstr. A.*, III, March 1945, 152.)

2. "Studies in X-ray pelvimetry. An evaluation of pelvic radiography, with a plea for simplicity." O. S. Heyns. *Journ. Obstet. and Gynaecol. Brit. Emp.*, April 1945, LII, 148-73.

3. "Vaginal cytology in premature puberty." A. A. Quinet. *An. Brasil Ginec.*, 1944, XVIII, 102. (*Int. Abstr. Surg.*, March 1945, LXXX, 197.)

PHYSIOLOGY

4. "La pretendida diferencia defensiva del peritoneo en los distintos sectores del abdomen." (The alleged differential defensive zones of the peritoneal cavity.) C. Stajano. *Obstet. y Ginec. Latin-Amer.*, December 1944, II, 927-40.

5. "The comparative effects of progesterone, estradiol, diethylstilbestrol and its monomethyl ether on the early blastocyst of the rabbit." N. T. Wertheissen, S. L. Gargill, S. Beriman and B. Greenberg. *Endocrinology*, February 1945, XXXVI, 110-17.
6. "Origin of ova and follicle cells from the germinal epithelium of ovary of albino rat as demonstrated by selective intravital staining with India ink." J. S. Latta and E. S. Pederson. *Anat. Rec.*, 1944, XC, 23-35. (*Brit. Abstr. A.*, III, February 1945, 82.)
7. "Development and degeneration of ovum and follicle as observed by intravital staining." E. O. Strassmann. *Amer. Journ. Obstet. and Gynecol.*, March 1945, XLIX, 343-55.
8. "The interrelationship between vitamins B and C and the female sex hormones in their action on the sex organs of the ovariectomized rat." V. Korenchevsky and K. Hall. *Journ. Path. and Bact.*, January 1945, LVII, 141-3.
9. "Ovarian stimulation by oestrogens. II. Stimulation in the absence of hypophysis, uterus and adrenal glands." P. C. Williams. *Journ. Endocrinology*, January 1945, IV, 125-6.
10. "Studies of the biological action of serum gonadotrophin. I. Decline in ovarian response after hypophysectomy. II. Ovarian response after hypophysectomy and oestrogen treatment. III. Role of endogenous gonadotrophin." P. C. Williams. *Journ. Endocrinology*, January 1945, IV, 127-30, 131-6, 137-42.
11. "Induction of heat in spayed female guinea pigs by subcutaneous hormonal implants." P. Bacsich and G. M. Wyburn. *Nature*, April 7th, 1945, CLV, 430.
12. "The role of the thyroid gland and oestrogen in the regulation of gonadotrophic activity of the anterior pituitary." J. P. Chu and S. S. You. *Journ. Endocrinology*, January 1945, IV, 115-24.
13. "The relationship of the normal and hyperactive ovary to menstruation and to endometrial hyperplasia." C. G. Hartman. *Journ. Clin. Endocrinology*, February 1945, V, 99-106.
14. "The basal metabolic rate of the American negro, with particular reference to the effect of menstruation on the female." U. S. Maxwell and G. Wakeham. *Journ. Nutrition*, April 1945, XXIX, 223-7.
15. "Interprétation des cycles dits 'anovulaires' chez la femme." (Interpretation of "anovular" cycles in women.) G. Dubreuil. *Gynéc. et Obstét.*, 1944/5, XLIV, 61-5.
16. "Time relationships of deciduomata formation in prolactin-treated and normal pseudopregnant rats." K. L. Sydnor. *Endocrinology*, February 1945, XXXVI, 88-91.
17. "The action of some spasmolytic substances on uterine motility." G. Lehmann. *Journ. Exper. Pharm. and Therap.*, January 1945, LXXXIII, 86-9.

PREGNANCY

GENERAL

18. "Obstetrics and gynaecology. Critical review." A. Leyland Robinson. *Brit. Encyclopaedia of Medical Practice, Medical Progress*, 1945, 16-24.

NORMAL

Physiology

19. "The influence of the thyroid on pregnancy and parturition in the rabbit." J. P. Chu. *Journ. Endocrinology*, January 1945, IV, 109-14.

20. "Growth and transformation of epithelium of gravid rabbit uterus outside the organism." Z. Schemkova. *C. R. Acad. Sci., U.S.S.R.*, 1943, XLI, 135-6. (*Brit. Abstr. A.*, III, March 1945, 174.)

21. "A propos de la réaction décrite par Mlle Grimaldi, dans les urines." (The urinary reaction described by Mlle. Grimaldi.) G. Chappaz. *Soc. Gynéc. Obstét.*, Paris, January 1944. (*Gynéc. et Obstét.*, 1944, XLIV, 13-4.)

22. "The biological conversion of cholesterol to pregnanediol." K. Bloch. *Journ. Biol. Chem.*, February 1945, CLVII, 661-6.

23. "Limitations of the correlation between the red cell volume and hemoglobin of blood during pregnancy." J. W. Mull. *Journ. Lab. and Clin. Med.*, March 1945, XXX, 278-9.

24. "Lipids in maternal and foetal blood plasma of sheep." J. Barcroft and G. Popják. *Journ. Physiol.*, March 1945, CIII, 32-3 P.

25. "Vaginal cornification phases during pregnancy—their prognostic significance." G. J. Hall. *Journ. Clin. Endocrinology*, January 1945, V, 34-7.

26. "La fisiologia de la placenta." (Physiology of the placenta.) L. P. Casanova. *Rev. españ. Obstet. y Ginec.*, February 1945, II, 89-98.

27. "Experimental foetal death: the surviving placenta." A. St. G. Huggett and J. J. Pritchard. *Proc. Roy. Soc. Med.*, April 1945, XXXVIII, 261-6.

Diagnosis.

28. "Early signs of pregnancy revealed by genital examination." R. D. Sisco and O. Agüero. *Rev. de Ginec. e d'Obstet.*, 1943, III, 189-97. (*Amer. Journ. Obstet. and Gynecol.*, February 1945, XLIX, 303.)

29. "A critical survey of two diagnostic pregnancy tests." (Colostrum intracutaneous and histidine tests.) J. F. Davey and D. E. Daley. *Canad. Med. Assoc. Journ.*, April 1945, LII, 371-6.

30. "The bitterling test" (letter). W. Fleischmann and S. Kann. *Journ. Clin. Endocrinology*, January 1945, V, 53.

Antenatal care, examination.

31. "A negro demonstration center for maternal and newborn care in Alabama." T. M. Boulware, E. LaForge and R. C. Stewart. *Southern Med. Journ.*, December 1943, XXXVI, 784. (*Amer. Journ. Dis. Childr.*, March 1945, LXIX, 182.)

32. "Some antenatal problems in a native village." *Sth. Afr. Med. Journ.*, March 10th, 1945, XIX, 77-8.

33. "A propos de quelques attitudes de déflexion foetale in utero." (Some abnormal positions of the foetus in utero.) J. Grasset. *Soc. Gynéc. Obstét.*, Paris, March 1944. (*Gynéc. et Obstét.*, 1944, XLIV, 35-8.)

See also Ref. 2.

Nutrition

34. "Importance of adequate protein nutrition in pregnancy." P. F. Williams. *Journ. Amer. Med. Assoc.*, April 21st, 1945, CXXVII, 1052-5.

35. "Ascorbic acid content of liver in pregnant mice." E. L. Kennaway and N. M. Kennaway. *Cancer Res.*, 1944, IV, 704-6. (*Brit. Abstr. A.*, III, February 1945, 105.)

See also Ref. 40.

ABNORMAL

Toxaemias

36. "Sobre exploración funcional renal en grávidas y puerperas." (Renal function in pregnancy and the puerperium.) J. P. Orfila. *Arch. Urug. Med.*, October 1944, XXV, 384-95.

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38. "Renal function tests in pregnancy." V. I. Krieger. *Med. Journ. Austr.*, March 24th, 1945, I, 290-7. Discussion, 309-10.

39. "Hemotherapy in pernicious vomiting." H. Duek. *An. Brasil de Ginec.*, 1944, XVII, 197-203. (*Amer. Journ. Obstet. and Gynecol.*, March 1945, XLIX, 444.)

40. "The relation of vitamin B₁ deficiency to the pregnancy toxaemias. A study of 371 cases of beri-beri complicating pregnancy." G. King and L. T. Ride. *Journ. Obstet. and Gynecol. Brit. Emp.*, April 1945, LII, 130-47.

41. "Placental changes in toxemia of pregnancy" (letter). R. S. Siddall. *Amer. Journ. Obstet. and Gynecol.*, February 1945, XLIX, 304.

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The Behaviour of the Foetus in Utero with Special Reference to the Incidence of Breech Presentation at Term

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THIS paper is, in some respects, a sequel to one published by the author in 1940¹, in which it was shown that the conditions causing diminution of the pelvic cavity were not the real causes of breech presentation at term. It was, at that time, put forward that the cause should be sought in those conditions which prevented spontaneous version from taking place. In some ways also this paper is an amplification of that theme. In the earlier paper the argument centred around the clinical impression that spontaneous cephalic version tended to take place during pregnancy in breech cases. It was felt necessary to collect more accurate information on this point. While doing this, the contention that breech presentations were not associated with abnormalities in, or of, the pelvis, could be re-tested, as also could the alternative contention that the breech presentation is associated with the extended attitude, with multiple pregnancy, and with prematurity.

The fundamental problem of why the foetus should present by the head rather than by the breech is one which still awaits solution. It has attracted a certain amount of speculation, but the theories advanced to explain it are not convincing. There are

the "accommodation" theories, and the theory of gravity.

1. *Accommodation of the foetus to the pelvis.*

Arguing from what is, in fact, a false premise, namely that when the pelvic brim is distorted, or is impinged upon by tumour, the foetus presents as a breech, an explanation is provided in that the circumference of the head is (on average) 13 inches, while that of the breech is only 11 inches. Therefore the latter engages.

Even supposing that the premise were not false, the measurements quoted are of the foetus at term, yet the breech may present at such a stage of prematurity that the head must measure considerably less than the figure given. Furthermore, the ultimate position of the foetus is in most cases decided long before the foetus makes any real attempt to enter the brim.

2. *Accommodation of the foetus to the uterus.*

The uterus is pyriform, wide above and narrow below. Whether the uterine walls can or cannot exert an influence on the position of the foetus will depend on the quantity of liquor in the amniotic sac. Suppose the quantity to be small—then the

narrower end of the foetus accommodates itself in the pelvis, and the wider in the fundus. This might account for the greater incidence of breech in the premature foetus, for the head is relatively larger than it will be at term. This theory might suffice for the primigravida, though it is difficult to believe that the distended uterus of late pregnancy does control the foetus so accurately, but in the case of the multigravida and in hydramnios it is scarcely tenable.

3. *The gravity theory.*

It is suggested that the head being the heavier end of the foetus, it will naturally tend to turn to a vertex as pregnancy proceeds. Against this, the head is relatively much heavier in the premature foetus than it is at term, yet the breech is much more common before the 30th week than after it. Furthermore the upright position is not constantly maintained by the pregnant woman, yet spontaneous cephalic version will also take place at the appropriate time in a woman confined to her bed for some coincident condition.

None of these theories is good enough, and as stated earlier, the problem still awaits solution.

I have suggested that for some reason, at present unknown, the foetus preferring to be born as a vertex, will undergo a version if it possibly can, and furthermore it will do so at the appropriate time unless it is prevented from doing so. Polak² puts the same point thus: "It would have been a head, if it could have been a head." This does not advance our knowledge of why the foetus tends to present by the head, but the corollary suggests why the foetus presents as a breech. The factors which prevent version are the factors which cause the breech presentation (normal earlier), to persist until term.

In the short statistical review published in March 1940,¹ 969 case records of breech

deliveries at 5 different maternity hospitals were examined, and it was found that disproportion was present only 13 times (1.3 per cent), and placenta praevia 31 times (3.2 per cent). Anencephaly was present 11 times, and hydrocephalus 9 times. In some of the cases of anencephaly and in many of placenta praevia prematurity was also a factor to be reckoned with, but even disregarding this, a pelvic anomaly could be found only in 6.7 per cent of these 969 breech cases. In the same series it was shown that in 387 cases of placenta praevia the foetus presented as a vertex 356 times, and only 31 times as a breech. In the same series, prematurity was present in 89 cases (9.1 per cent), multiple pregnancy in 229 (23.6 per cent). The extended attitude was recorded 362 times (37.3 per cent). In 222 instances no abnormality was recorded. It was on these figures that I based the hypothesis that the breech presentation should be regarded as a persistence beyond the stage in pregnancy when to present by the breech is normal, and that the persistency is due to those factors which prevent spontaneous cephalic version from taking place.

It has been argued by Gibberd in a personal communication that the foetus extends its legs, because it is a breech. This is the "accommodation theory" in another guise, the suggestion being that the foetus, unable to get the breech and feet together into the pelvis, gets the latter out of the way. There is evidence, however, which suggests that the extended attitude of these foetuses is of long standing. He has quoted Trillat's description of two cases of congenital torticollis and attributes this to muscle spasm. In my opinion it is an under-development caused by the head being on one side *in utero* for a long time, and kept in position by the extended limbs. I have seen congenital torticollis in an elderly primigravida delivered by Caesarean section. I have also seen, and a photo-

graph is shown of, a baby in whom the long continued pressure of the extended arm caused a deep indentation of the skull. Chapple and Davidson⁴ show that many congenital malformations are associated with the abnormal foetal position *in utero*. They instance congenital dislocation of the hip, hyperextension of the knee ("back-knees"), facial asymmetry, and torticollis. For these gross abnormalities to take place the faulty attitude of the foetus must surely have been of long standing, and have occurred before that stage in gestation when the presence of the feet would make it impossible for the breech also to be accommodated in the pelvis.

To get more light on spontaneous movements of the foetus I set myself the task of documenting my observations on a consecutive series of antenatal patients until such time as the foetus had been observed to present as a breech in 1,000 instances.

Believing that clinical diagnosis could not be made with any certainty in an adequate percentage of cases much earlier than the 30th week, this was about the stage at which I elected to make my first examination. The patients had all been seen earlier than this and any observations then made were used. They were also seen, subsequently, by myself if I wished, and by others if not, and again any relevant data were added. As a check on clinical diagnostic precision, the presentation at birth was also noted. In this way observations covering the whole period when palpation is of value, were gradually accumulated. After 3½ years this part of the task was finished. One thousand breech presentations had been observed after 3,875 patients had passed through our hands, and mainly through my own. Skiagrams were taken if the diagnosis was in doubt, though this was not often. They were also taken in many instances of failed version.

Here then were figures by which certain hypotheses could be checked, upon which observations could be made, and from which certain conclusions could, with justification I hope, be drawn. It may help if at this stage I list these *seriatim*. They will be discussed more fully in the matter which follows.

The Nine Postulates.

(1) The incidence of the breech presentation at the 30th week is high.

(2) In most breech cases, spontaneous version takes place.

(3) Spontaneous cephalic version is a manœuvre which tends to take place once, and once only.

(4) Spontaneous cephalic version is only very rarely followed by a reversion.

(5) Spontaneous cephalic version takes place at a specific time in pregnancy.

(6) Spontaneous podalic version is not common.

(7) External version has a higher reversion rate than has spontaneous version.

(8) Failed version is associated with certain definite clinical findings.

(9) Unheralded breech presentation at term cannot be eliminated, for reasons which will appear later in the text. It too is associated with definite, though different clinical findings.

I. THE INCIDENCE OF BREECH PRESENTATION.

The incidence of breech presentation is high. One thousand breech presentations were observed after 3,875 patients had passed through the clinic.

One woman in 4 therefore is known to have a breech at some time or other. It may well be that an even greater number occur. To prove this would necessitate repeated skiagrams being taken, a formidable task in peacetime, and quite out of the question in time of war. It is hoped that

evidence on this point can be accumulated gradually.

Dearnley⁵ with many others agrees "that breech presentation is common till the 34th week."

TABLE I.
Parity and Breech Presentation.

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 |
|-----|-----|----|----|----|---|---|---|---|----|----|
| 523 | 309 | 85 | 25 | 12 | 4 | 1 | 4 | 1 | 1 | 1 |

Parity does not seem to be an important factor, 523 of the patients were primiparae, 443 were multiparae. (The information as to parity is missing in some of the earlier cases.)

Breech presentation is thus so common that it must be regarded as a normal occurrence at certain stages in pregnancy.

Ryder⁶ analysing 1,721 cases finds 272 breeches, an incidence of 1 in 6.

2. SPONTANEOUS CEPHALIC VERSION.

In most breech cases spontaneous cephalic version takes place. This movement was observed on 680 occasions:

TABLE II.

| | | | | | |
|----------------------------|-----|-----|-----|-----|-------|
| As a single process | ... | ... | ... | 599 | times |
| In 5 cases occurring twice | ... | ... | ... | 10 | " |
| Followed by SPV and EV | ... | ... | ... | 16 | " |
| After SPV | ... | ... | ... | 11 | " |
| Followed by SPV and FV | ... | ... | ... | 3 | " |
| After SPV, EV and SPV | ... | ... | ... | 1 | " |
| After SPV and FV | ... | ... | ... | 2 | " |
| After EV and SPV | ... | ... | ... | 10 | " |
| After repeated EV and SPV | ... | ... | ... | 2 | " |
| After FV | ... | ... | ... | 26 | " |
| Total | | | | 680 | " |

SPV = Spontaneous podalic version

EV = External version

FV = Failed version

Thus in 1,000 cases observed spontaneous version occurs 680 times, and in 599 instances this is the only movement which the foetus is seen to undergo. Of the remaining 81 cases there is clinical inter-

ference in 60 instances which makes it impossible to say what would have happened had they been left alone, but as it stands this table shows that spontaneous cephalic version is a movement which only very rarely takes place twice, only 5 times in these 1,000 cases.

The influence of parity seems to be unimportant. In the 599 cases in which the movement of spontaneous cephalic version was the only one known to have taken place, 312 are primiparae, and 287 multiparae.

Polak,⁷ criticizing the operation of external version, makes the point that "it would have been a head if it had been left alone."

Taussig⁸ states that "with a normal pelvis, normal uterus, and a single foetus,

TABLE III.

Parity and Spontaneous Cephalic Version.

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 |
|-----|-----|----|----|---|---|---|---|---|----|----|
| 312 | 206 | 55 | 13 | 7 | 1 | 1 | 1 | 1 | 1 | 1 |

gravity and the kicking movements almost always tend to the vertex presentation."

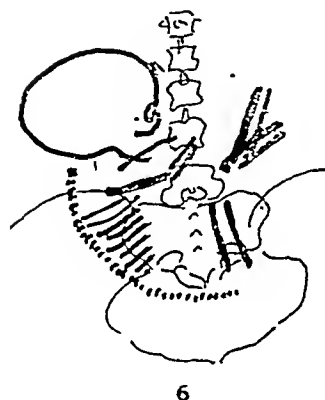
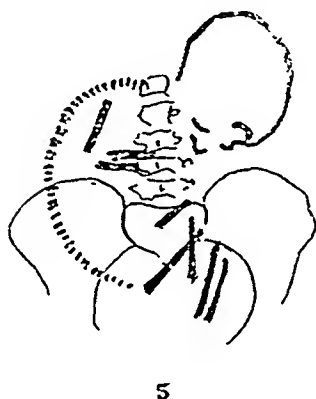
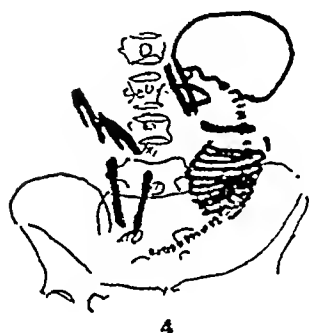
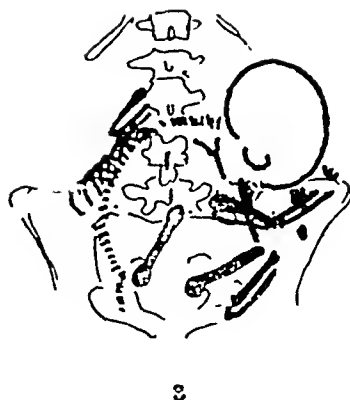
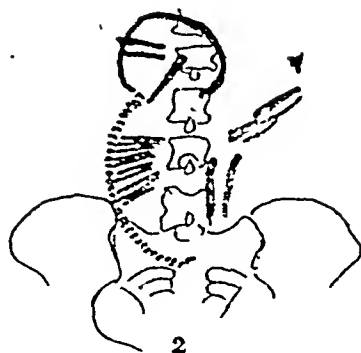
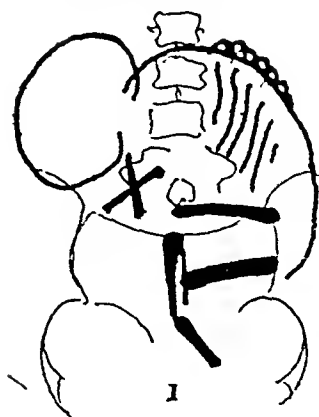
They agree therefore that a vertex usually results spontaneously. Taussig's reasons need further investigation.

Ryder⁶ on the other hand found that only 15 out of 258 breeches underwent spontaneous version, but in his series external version was performed 214 times. It seems that Polak was right in suggesting that his figure was lower than it would have been, had the operation been left till later.

Plates 1 to 9 are drawings from skiagrams of foetuses which underwent spontaneous version.

3. THE TIME AT WHICH SPONTANEOUS VERSION TAKES PLACE.

Spontaneous version takes place at a specific time in pregnancy. It is not easy however to elucidate this, for we must face the fact that we do not know exactly how



PLATES 1 TO 9.

Drawings from skiagrams of foetuses which underwent spontaneous cephalic version. All skiagrams taken are shown. It should be noted that the general pattern is one of flexion.

- In Plates 1, 3, 5, and 8 ... full flexion.
- In Plates 2, 6, and 7 ... semi-flexion.
- In Plates 4, and 9 ... extension.

advanced pregnancy is when we examine a patient. We are not dealing with laboratory animals impregnated on a known date. We have to deduce the stage of pregnancy from the date of the last menstrual period. In this series I have deducted 3 months and added 7 days to the 1st day of the last menstrual period irrespective of the particular months involved. When it is noted that a patient is at this or that week it is appreciated that one may be at least 2 weeks out in the calculation. Curiously enough, however, patients do deliver them-

taken place by the 34th week. Certainly many have taken place before this, and the figure for those completed by the 32nd week should probably be higher.

Table IV shows that it is most common to find spontaneous version to be completed by the 32nd week, with the 31st and 33rd weeks coming next. These 3 weeks are apparently the critical weeks, and bearing in mind what has been said about the limitations imposed on accuracy, I submit that it will not be easy to fix the date more accurately than this.

TABLE IV.

Showing the Stage of Pregnancy, in Weeks, by which Version is known to have Taken Place.

| 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 |
|----|----|----|----|----|----|-----|-----|-----|----|----|----|----|----|----|----|
| 1 | 1 | 6 | 10 | 19 | 69 | 118 | 133 | 100 | 60 | 18 | 10 | 4 | 1 | - | 9 |

selves fairly near to the calculated date. I do not believe that the height of the fundus is of any value in this respect. When one pauses to consider that the weight of the foetus at term may vary from 5 to 10 pounds, and that the quantity of liquor may be 2 or 10 pints one realizes the limitations of this observation in assessing the duration of pregnancy in terms of weeks.

The second inescapable fact is that we cannot say when spontaneous version takes place, but only by what date it is known to have taken place.

Subject to these two limitations however it is possible to arrive at an estimated date.

Dearnley² states that spontaneous version often occurs up to the 34th week. Ryder notes that it takes place between the 6th and 7th months (presumably between the 27th and 31st weeks). His work was done, however, to eliminate the breech at term, and his external versions were done earlier than in the present series. The bulk of his spontaneous versions were thus anticipated.

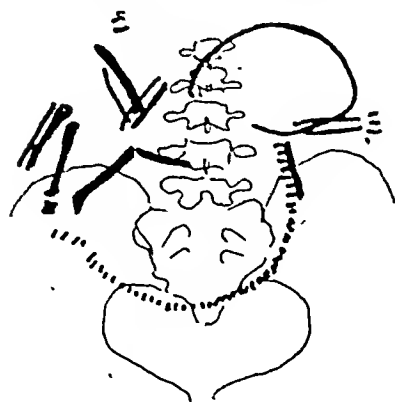
In the present series the bulk of the spontaneous versions are known to have

4. REVERSION.

Spontaneous cephalic version is only rarely followed by a reversion. This is an important finding, for it is still widely held that the foetus is constantly travelling around in the amniotic sac, and is dependent on "chance," or "gravity" or "frequent kicking movements" for its ultimate position. This is quite certainly not so, for, in this series, while in 599 cases spontaneous version was the only observed movement, in only 25 other cases was this version followed by a reversion to a breech. This suggests to me that the foetus has made a purposive movement, for some definite reason.

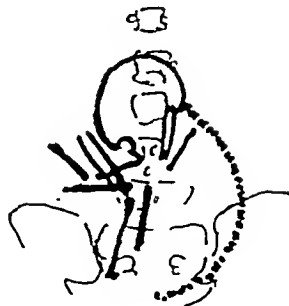
The fate of these 25 reversions is as follows: 5 underwent a second spontaneous version; 16 had an external version performed in the interests of the patient; 1 had external version performed twice (we cannot say what would have happened to these 17 had they been left); 3 went to term as breech cases.

The number (25) is too small to study the influence of parity on this tendency to revert. The figures for what they are worth



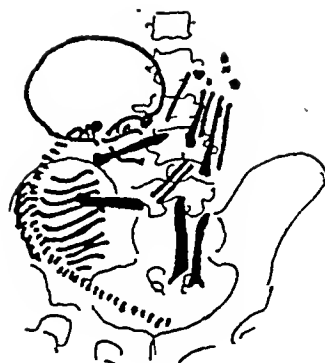
10

Gravida 3.
EV at 29 weeks.
SPV at 30 weeks.
SV at 33 weeks.
Skiagram at 30 weeks.



11

Gravida 1.
EV at 33 weeks.
SPV at 34 weeks.
SV at 36 weeks.
Skiagram at 34 weeks.



12

Gravida 2.
EV at 32 weeks.
SPV at 32/33 weeks.
EV at 33 weeks.
SPV at 33/36 weeks.
SV at 38 weeks.
Skiagram at 37 weeks.

PLATES 10 TO 12.

From skiagrams of the foetuses which had been subjected to external version, and which had reverted to breech. Plate 11 is from a primigravida. Plates 10 and 12 are from multigravidae. It is seen that the foetuses have more room for movement in these cases.

All these subsequently underwent spontaneous cephalic version.

are given in Table V. They seem to show that the manoeuvre is more likely to take place in the multipara.

TABLE V.

| | Primiparae | Multiparae | Total |
|-----------------------|------------|------------|-------|
| SV. SPV. SV | 1 | 4 | 5 |
| SV. SPV. EV | 6 | 10 | 16 |
| SV. SPV. EV repeated | 1 | — | 1 |
| SV. SPV. FV. B | 2 | 1 | 3 |
| Total | 10 | 15 | 25 |

SV = Spontaneous cephalic version

EV = External version

FV = Failed version

It is true that the patients were not examined every day, but the impression that these figures reveal the correct state of affairs is strong. Reversions should have been much more commonly observed if they had indeed occurred.

Herbert Spencer observed that after $7\frac{1}{2}$

months the foetus rarely changed its position. We do not know if these were lunar or calendar months; assuming the latter, then one month contains 4 weeks and 3 days approximately, so that $7\frac{1}{2}$ months equals 33 weeks.

Plates 10 to 12 are from skiagrams taken after reversion to breech.

5. SPONTANEOUS PODALIC VERSION.

Spontaneous podalic version was observed to occur 134 times thus:

TABLE VI.

| | | |
|--|-----|-------|
| After spontaneous cephalic version ... | 25 | times |
| After SCV, SPV, and EV | 1 | " |
| As an initial movement (i.e. reported to be a vertex before the 30th week) ... | 45 | " |
| After one external version | 16 | " |
| In 32 cases of repeated EV | 46 | " |
| After 1 FV, and 1 successful EV ... | 1 | " |
| Total | 134 | " |

This movement is thus seen to occur 134 times in 3,875 patients or in 3.46 per cent of cases. If then the foetus reaches the 31st to 33rd week as a vertex the chance of this presentation being disturbed is remote.

TABLE VII.

Cases in which Spontaneous Podalic Version was the Initial Movement.

| | | | | | | |
|------------------|-----|-----|-----|-----|-----|----|
| SPV. SV | ... | ... | ... | ... | ... | 11 |
| SPV. EV | ... | ... | ... | ... | ... | 20 |
| SPV. EV. SPV. SV | ... | ... | ... | ... | ... | 1 |
| SPV. FV. SV | ... | ... | ... | ... | ... | 2 |
| SPV. FV. B | ... | ... | ... | ... | ... | 4 |
| SPV. B | ... | ... | ... | ... | ... | 7 |
| Total | | | | | | 45 |

It was noted to occur as an initial movement on 45 occasions; one quarter of these readjusted themselves. Half were corrected and again we cannot say what would have been their fate. The remaining

delivered as a vertex, have not been extracted from the records.

Randall⁹ suggests that an X-ray photograph should be taken after a spontaneous podalic version "as an anomaly of the foetus may be detected."

In this series, with the exception of the first, there is no suggestion of any factor influencing the foetus.

6. EXTERNAL VERSION AND REVERSION.

External version has a higher reversion-rate than has spontaneous version; a fact which suggests that the obstetrician is not so clever as the foetus in deciding when the operation should be done. The inability to date the stage of pregnancy accurately is one factor in this.

In this series the operation was performed 330 times (Table IX).

In the categories marked with an aster-

TABLE VIII.

| Number | Age (years) | Gravida | Vertex noted | Breech first noted |
|--------|-------------|---------|--------------|----------------------------------|
| 1090 | 23 | 1 | 34 | 42 (anencephaly and spinabifida) |
| 477 | 33 | 1 | 30 | 39 |
| 332 | 19 | 1 | 40 | 40 |
| 994 | 29 | 1 | 33 | 38 |
| 1155 | 30 | 1 | 36 | 37 |
| 368 | 37 | 2 | 29 | 33 |
| 667 | 25 | 1 | 36 | 37 |
| 1122 | 23 | 1 | 31 | 35 |
| 828 | 21 | 1 | 33 | 38 |
| 671 | 44 | 3 | 36 | 38 |
| 1404 | 23 | 1 | 34 | 40 |

quarter went to term as a breech (Table VII).

The details are here given of the 11 cases in which spontaneous podalic version occurred, and when the patient went to term as a breech (Table VIII).

The details of those starting with an SPV and of those cases in which an SPV was noted, but which were subsequently

isk, this interference was successful, and no reversion occurred (223). In the categories marked † the final EV was successful (35). The total number of ultimately successful external versions is thus 258. In the remaining cases something else happens afterwards. The reversion-rate is thus 22 per cent approx.

Ryder⁶ finds also that one third of the



Photograph of a baby born as a breech with extended limbs. There is marked compression of the skull, and facial asymmetry.

C.K.V.

external versions performed will revert (33.3 per cent).

McGuinness¹⁰ in a short series shows 12 reversions in 57 external versions (21 per cent).

The weeks at which a successful and

TABLE IX.

| | |
|---------------------------------|------|
| *SV. SPV. EV | 15 |
| †SV. SPV. EV. repeated once ... | 1 |
| † do. do. repeated thrice ... | 1 |
| *SPV. EV | 20 |
| SPV. EV. SPV. SV | 1 |
| *EV | 176 |
| EV. SPV. SV | 10 |
| †EV. repeated once | 23 |
| †EV. repeated twice | 6 |
| †EV. repeated thrice... .. | 3 |
| EV. repeated once, SPV. SV ... | 2 |
| EV. SPV. B | 6 |
| *FV. EV | 12 |
| †FV. EV. repeated thrice | 1 |
| Total | 330. |

SV = Spontaneous cephalic version

final version was performed in the above mentioned 258 cases as shown in Table X. The weeks at which external versions are done in those cases where the cephalic position is not maintained is also shown. Table XI.

TABLE X.

| 22 | 23 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 |
|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| 1 | 1 | 4 | 2 | 9 | 7 | 11 | 14 | 49 | 47 | 36 | 29 | 28 | 10 | 5 | 2 | 3 |

TABLE XI.

| Week | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 |
|--------|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Number | 1 | 1 | 4 | 5 | 10 | 11 | 16 | 10 | 5 | 4 | 2 | 2 | 1 |

TABLE XII.

| Week | 22 | 23 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 |
|--|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Finally | | | | | | | | | | | | | | | | | |
| successful version | | 1 | 1 | 4 | 2 | 9 | 7 | 11 | 14 | 49 | 47 | 36 | 29 | 28 | 10 | 5 | 2 |
| Version not final | | | | | 1 | 1 | 4 | 5 | 10 | 11 | 16 | 10 | 5 | 4 | 2 | 2 | 1 |
| Approximate percentage of versions which are not final | | | | | 33 | 10 | 36 | 31 | 41 | 18 | 25 | 21 | 15 | 13 | 16 | 28 | 25 |

Examining Table XI it is seen that the incidence of reversion begins to fall off after the 33rd week.

This can also be expressed in percentage by combining Tables X and XI.

The tendency is for a high percentage of versions performed early to revert, while after the 31st week this tendency falls off.

7. FAILED VERSION.

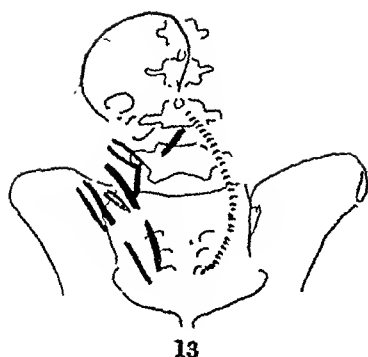
Failure to turn the breech to a vertex occurred on 77 occasions, thus:

TABLE XIII.

| | |
|-----------------------|----|
| SV. SPV. FV. B | 1 |
| SPV. FV. SV | 2 |
| SPV. FV. B | 6 |
| EV. SPV. FV. B | 3 |
| FV. SV | 26 |
| FV. EV | 12 |
| F.V. repeated | 1 |
| FV. B | 26 |
| Total | 77 |

The failure was subsequently overcome, spontaneously 28 times, and by the obstetrician 13 times. In the remaining 36 instances the patient was delivered as a breech.

Plates 13 to 16 are of drawings from skiagrams of foetuses in which version failed,



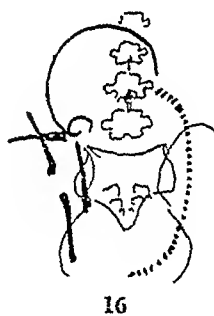
Gravida I.
FV at 33 weeks.
SV 33/34 weeks.
Skiagram at 33 weeks.



Gravida I.
FV at 34 and 36 weeks.
SV 36/40 weeks.



Gravida I.
FV at 31 weeks.
Skiagram at 33 weeks.
SV at 33/34 weeks.



Gravida I.
FV at 34 weeks.
Skiagram at 35 weeks.
SV 35/40 weeks.

PLATES 13 TO 16.

From skiagrams taken after failed version. In all these cases spontaneous version followed.

The attitude is extension in 13, 14, and 16.

The attitude is flexion in 15.

and in which spontaneous version subsequently occurred (FV. SV.).

There were 2 stillbirths. In No. 4 Spalding's sign was noted when she was X-rayed and she delivered herself of a macerated hydrocephalic. In No. 22 the mother had albumen "++" in the urine, and BP 165/120 (see Table XIV).

Vaginal bleeding occurred after attempted version in Cases 18 and 35.

Very little liquor was noted in Cases 39, 27.

Case 29 was a multiple pregnancy.

Case 23 was the patient's 2nd breech delivery.

The table of cases of failed version result

TABLE XIV.

Details of Breech Deliveries after Failed Version (36 cases).

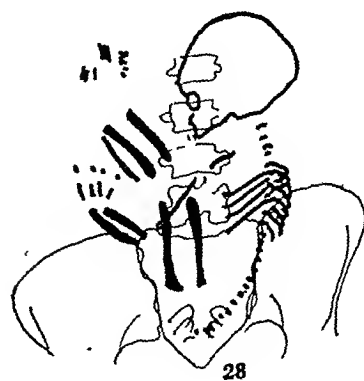
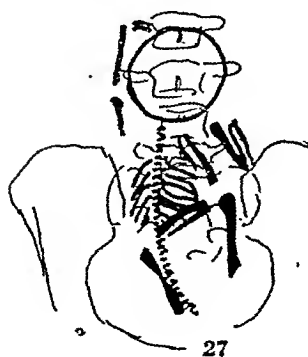
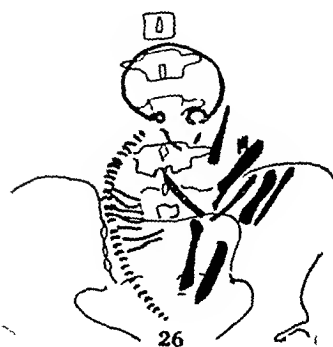
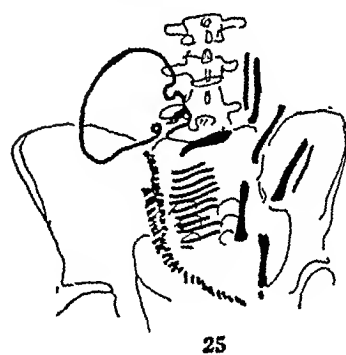
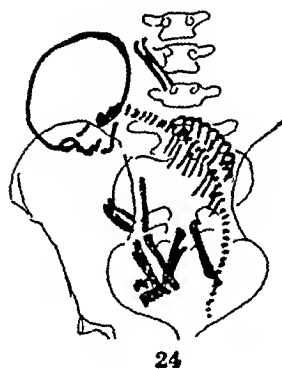
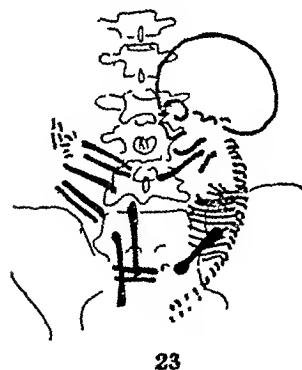
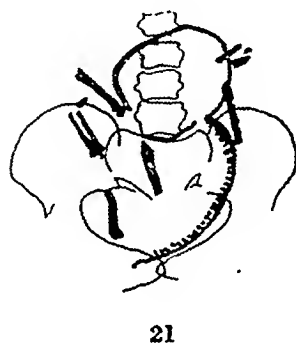
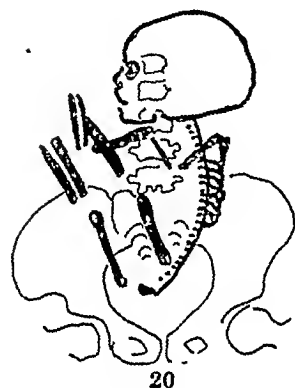
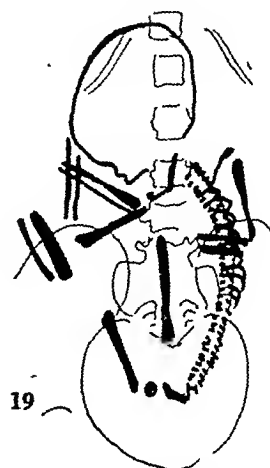
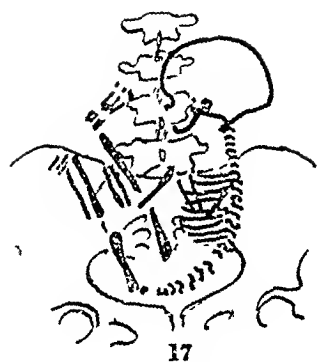
| No. | Case number | Age (years) | Gravida | Maturity (weeks) | Weight of baby lb. oz. | Attitude | X-ray | Anaesthetic | Treatment | Fate of baby |
|-----|-------------|-------------|---------|------------------|------------------------|--------------------------|-------|-------------|-----------|--------------|
| 1. | 998 | 22 | I | 38 | 5 12½ | Extd. legs | o | + | ARM | A |
| 2. | 69 | 28 | I | 40 | 6 7½ | do. | + | o | ARM | A |
| 3. | 1137 | 35 | I | 38 | 3 10 | do. | + | | | A |
| 4. | 498 | 19 | I | 35 | 7 0 | do. | + | | | SB |
| 5. | 856 | 23 | I | 40 | 6 15 | do. | + | + | | A |
| 6. | 1389 | 24 | I | 38 | 6 1¾ | do. | + | | | A |
| 7. | 16 | 22 | I | 39 | 6 0¾ | do. | + | + | | A |
| 8. | 85 | 26 | I | 39 | 7 1½ | do. | + | | ARM | A |
| 9. | 214 | 26 | I | 38 | 6 2 | do. | + | | | A |
| 10. | 470 | 30 | I | 39 | 7 1½ | do. | + | | | A |
| 11. | 1105 | 29 | I | 39 | 7 0¾ | do. | + | | ARM | A |
| 12. | 105 | 27 | I | 40 | 6 4½ | do. | + | | ARM | A |
| 13. | 202 | 20 | I | 38 | 5 7 | Well flexed | + | + | ARM | A |
| 14. | 994 | 29 | I | 39 | 6 3 | | | | M.Ind. | A |
| 15. | 368 | 37 | 2 | 40 | 7 0¾ | | | + | M.Ind. | A |
| 16. | 1022 | 23 | I | 37 | 6 3 | | | | | A |
| 17. | 636 | 20 | I | 37 | 6 0¼ | | | | | A |
| 18. | 160 | 29 | I | 36 | 5 5¼ | | | + | ARM | A |
| 19. | 740 | 32 | I | 38 | 6 2 | | | + | ARM | A |
| 20. | 325 | 26 | I | 40 | 7 13¾ | | | | | A |
| 21. | 576 | 28 | 2 | 38 | 6 10½ | Ext. limbs | + | | ARM | A |
| 22. | 735 | 27 | I | 39 | 6 6½ | 1 arm and 1 leg extd. | + | | | SB |
| 23. | 896 | 25 | 2 | 35 | | | | | | A |
| 24. | 706 | 34 | I | 37 | 6 8½ | Extd. legs | | | ARM | A |
| 25. | 862 | 25 | I | 36 | 6 1 | do. | | | | A |
| 26. | 1123 | 20 | I | 37 | 7 0¼ | do. | + | | M.Ind. | A |
| 27. | 1052 | 29 | 2 | 40 | 7 1¼ | do. | | | | A |
| 28. | 157 | 28 | I | 40 | | | | + | | A |
| 29. | 1011 | 29 | I | 40 | 5 3¼ | | | | | A |
| 30. | 825 | 21 | I | — | | | | | | |
| 31. | 671 | 44 | 3 | 40 | 6 3½ | | | | M.Ind. | A |
| 32. | 1404 | 23 | I | 40 | 7 11 | Extended | | | | A |
| 33. | 1110 | 16 | I | 38 | 6 8½ | Semi-extd. | + | | | A |
| 34. | 358 | 30 | 2 | 37 | 6 8½ | Extd. legs | + | | ARM | A |
| 35. | 1018 | 30 | 5 | 38 | 7 13½ | | | | | A |
| 36. | 611 | 29 | I | 38 | 6 9 | | | | | A |

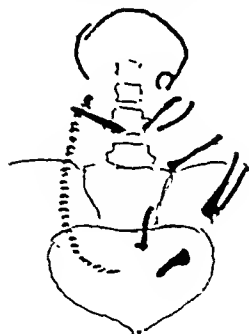
+ = Skiagram taken, or anaesthetic administered for version.

A = Born alive.

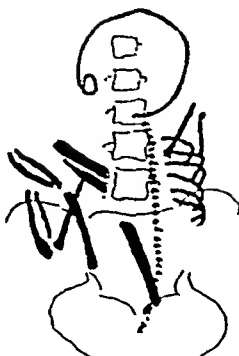
ARM = Artificial rupture of the membranes.

M.Ind. = Medical induction.





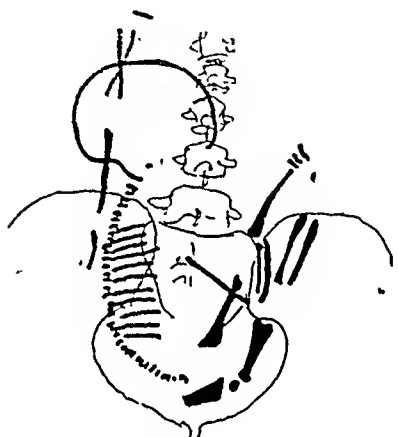
29



30



31



32



33

PLATES 17 TO 33.

From skiagrams taken after failed version. Breech persists till delivery.

The attitude is extension in:

17, 18, 20, 21, 22, 26, 28, 29, 30, 31, 32, 33.

The attitude is semi-extension in:

19, 23, 25, 27.

The attitude is flexion in 24.

The particularly upright stance in numbers 19, 20, 26, 27, 28, 29, 30 and 31 should be noted. It indicates a tight application of the uterus to the foetus and means that the quantity of liquor is small.

ing in breech delivery at term shows that in 20 of the 36 cases the attitude was extension, and in 1 other, semi-extension. Confirmation was made by skiagram in 16 instances, in 4 others the observation was made at delivery. In 15 cases there is no note of the attitude of the foetus.

Very little liquor was estimated to be present in 3 of the cases.

There was 1 instance of multiple pregnancy.

Five were multiparae and the remainder primiparae. (In 2 instances the information is lacking.)

An anaesthetic was administered for attempted version in 9 cases.

Reproductions of the skiagrams are shown (Plates 17 to 33).

BREECH DELIVERIES.

The number of women who were known to have a breech presentation at some time or other in their pregnancy and who were subsequently delivered as a breech was 85, or 8.5 per cent. The other 91.5 per cent are eliminated. This figure of 85 is made up as shown in Table XV.

TABLE XV.

| | | | | | | |
|----------------|-----|-----|-----|-----|-----|----|
| SV. SPV. FV. B | ... | ... | ... | ... | ... | 1 |
| SP. FV. B | ... | ... | ... | ... | ... | 6 |
| SPV. B | ... | ... | ... | ... | ... | 5 |
| EPV. B | ... | ... | ... | ... | ... | 2 |
| EV. SPV. B | ... | ... | ... | ... | ... | 3 |
| EV. SPV. FV. B | ... | ... | ... | ... | ... | 3 |
| F.V. B | ... | ... | ... | ... | ... | 26 |
| B | ... | ... | ... | ... | ... | 39 |
| Total | | | | | | 85 |

EPV = External podalic version.

TABLE XVI.

Unheralded Breech Deliveries (32).

| Number | Age (years) | Parity | Maturity (weeks) | Baby's weight lb. oz. | Attitude | Notes | Result to baby |
|--------|-------------|--------|------------------|-----------------------|----------|----------------------------|----------------|
| 723 | 23 | 1 | 39 | | | 1st of twins | A |
| 843 | 23 | 1 | 35 | 1 14 | | 1st of twins; macerated | SB |
| | | | | 2 7 | | 2nd of twins; macerated | SB |
| 63 | 31 | 1 | 38 | 5 0 $\frac{3}{4}$ | | 2nd of twins | A |
| 114 | 25 | 1 | 40 | v.small | | Macerated | SB |
| 162 | 37 | 4 | 36 | 4 6 | | Maternal BP 180/120 ARM | A |
| 974 | 24 | 1 | 38 | 7 2 | Extended | Very little liquor | A |
| 825 | 23 | 1 | | | | Transferred | |
| 1238 | 22 | 2 | 36 | 4 1 | | 1st of twins | A |
| 1271 | 28 | 2 | 37 | | | Macerated, small placenta | SB |
| 1223 | 37 | 3 | 29 | 2 4 | | Premature | D |
| 1274 | 26 | 3 | 40 | 6 13 | | 1st of twins | A |
| 870 | | | 34 | | | Transferred | |
| 7 | 21 | 2 | 31 | | | Premature | SB |
| 203 | 25 | 1 | 41 | 7 2 $\frac{1}{2}$ | | Hydrocephalus; spinabifida | A |
| 872 | 21 | 1 | 40 | 5 3 | Extended | Spinabifida; talipes | SB |
| 1229 | 32 | 1 | 40 | 6 1 $\frac{1}{2}$ | Extended | Undiagnosed | A |
| 415 | 27 | 1 | 32 | 5 7 | | Macerated; anencephalic | SB |
| 541 | 34 | 2 | 36 | 4 12 $\frac{1}{2}$ | | 2nd of twins | A |
| 578 | 27 | 2 | 38 | 5 6 | | 2nd of twins | A |
| 684 | 26 | 2 | 38 | 6 2 | | 1st of twins | A |
| 960 | 30 | 2 | 38 | | | One of twins | A |
| 411 | 42 | 1 | 36 | 4 4 | | 2nd of twins | A |
| 283 | 27 | 1 | 26 | not weighed | | 1st of twins | SB |
| | | | | | | 2nd of twins | SB |
| 1199 | 37 | 2 | 38 | 7 11 | | 2nd of twins | A |
| 939 | 26 | 2 | 40 | 6 2 $\frac{1}{2}$ | | Hypospadias | A |
| 365 | 32 | 1 | 40 | 5 0 | | 2nd of twins | A |
| 1042 | 35 | 5 | 26 | | | Macerated; premature | A |
| 178 | 37 | 3 | 30 | 2 7 | | Placenta praevia | SB |
| 73 | 35 | 5 | 36 | 8 1 $\frac{1}{4}$ | | | A |
| 1044 | 24 | 2 | 42 | 7 1 $\frac{3}{4}$ | | Little liquor | A |

With the exception of the external podalic versions followed by breech delivery, and of the cases of breech delivery without any recorded movements, either spontaneous or induced, these breech deliveries have been described earlier in the text. It remains only to enlarge upon these two exceptions.

External Podalic Version (2).

There were two cases in which this operation was performed. One was previously a brow presentation in a primigravida, the other was a sextipara with an oblique lie (Table XVI).

In addition to these 32 cases, there were 7 others the notes of which could not be traced. One was known to be a case of twins, and 1 a premature.

Rearranging Table XVI we see that the 32 breeches are made up as follows:

| | | | | | | |
|------------------------------------|-----|-----|-----|-----|-----|----|
| One of twins | ... | ... | ... | ... | ... | 15 |
| Premature or macerated | ... | ... | ... | ... | ... | 6 |
| Spinabifida (1 with hydrocephalus) | ... | ... | ... | ... | ... | 2 |
| (Anencephaly also macerated 1) | | | | | | |
| Nothing unusual | ... | ... | ... | ... | ... | 4 |
| Information lacking | ... | ... | ... | ... | ... | 2 |
| Little liquor | ... | ... | ... | ... | ... | 2 |
| Placenta praevia | ... | ... | ... | ... | ... | 1 |

There was 1 placenta praevia. The foetus was also premature.

STILLBIRTHS.

In Table XVI, where the information of 32 breech deliveries is complete, there are 11 stillbirths.

They are made up as follows:

| | | | | |
|------------------|-----|-----|-----|---|
| Macerated foetus | ... | ... | ... | 5 |
| Premature | ... | ... | ... | 5 |
| Abnormal foetus | ... | ... | ... | 1 |

One premature baby died subsequently.

In Table XVI, where the information of failed version there were 2 stillbirths, 1 was macerated, and in the other case the mother was severely toxic.

In the whole series therefore 13 stillbirths and 1 neonatal death occur. In 13 of these the chance of survival was hopelessly prejudiced. In the remaining 1 the maternal toxæmia must have prejudiced the chance of survival. There was no other foetal death. Fourteen foetal deaths thus occur in 87 cases (16 per cent).

As only 1 of these could have survived, the "delivery mortality" is 1.14 per cent or nil, according to how the influence of the maternal toxæmia in Table XIV, No. 22, is assessed.

DISCUSSION.

It is probably agreed that the incidence of breech at some time or other in pregnancy is high. It was surprising to find it so high, but as the notes of all patients passing through the clinic during the period of the investigation were perused, and the information used whether or not the patients had been seen personally, the question of selection is eliminated.

Breech presentation is regarded with too much apprehension by the patients. It should be possible, however, if medical students and midwives are correctly taught, to build up the concept that this presentation is normal at a certain stage in pregnancy. Such phrases as "the baby is upside down" (when incidentally it is in the position we all prefer), and that "the baby is the wrong way round," should disappear. No good can be done by causing an antenatal patient to think that there is something wrong, or that she is abnormal.

From the figure given earlier it can be anticipated that spontaneous version will take place in 3 out of 5 patients. The patients can be told this and they will look forward to having this confirmed at their next visit.

Why spontaneous version takes place requires further investigation. The fact that

it is usually a solitary movement, and that it takes place at a specific time in pregnancy, is against its being a purely chance phenomenon. If it is due to gravity then it would have to be shown that the specific gravity of the foetal head becomes progressively greater than that of the caudal end. This still would not explain why version takes place in the recumbent patient, or why the new position is sometimes reversed again.

Why spontaneous podalic version takes place is also an interesting speculation. It does not occur often enough to lend support to the theory that the foetus is constantly changing its position, and that therefore the choice of heads or tails at term is decided by chance. It is worthy of note that it happened in only 25 instances after spontaneous version, whereas it occurred 64 times after external version. It could be inferred that if the conditions necessary for cephalic version are not present then reversion may take place after an external version prematurely performed.

Why spontaneous cephalic version does not take place is more easily elucidated. Examination of Tables XIV and XVI, where the details of 68 cases are set out, shows the following facts:

| | | | |
|---|-----|-----|----|
| Extended attitude of the foetus (5 times associated with little liquor) | ... | ... | 23 |
| Twin pregnancy | ... | ... | 17 |
| Premature and/or macerated | ... | ... | 7 |
| Abnormal foetus | ... | ... | 3 |

In 50 out of the 68, therefore, there is something to consider, and it seems justifiable to postulate that, in the premature and the abnormal foetus, the conditions necessary for spontaneous version have not yet occurred, and that, in the cases in which the limbs are extended and when there is little liquor, the foetus can no more get round than can the obstetrician force it round. When twins are present the foetuses

may mutually prevent each other from turning.

In this series these are the causes of the breech presentation. Contracted pelvis, fibroid or ovarian cyst were not found. Only 1 placenta praevia was noted and prematurity was a coincident factor.

Stein¹¹ of Chicago notes the frequency of the extended attitude in breech cases, and its relative infrequency in vertex cases and has speculated that this may be one of the causes of breech presentation. He points out that in an analysis of skiagrams taken in late pregnancy, and in labour, the attitude of deflexion is the rule.

Henderson¹² of Detroit found "the extended attitude" (meaning extended legs) in approximately 75 per cent of cases.

When spontaneous cephalic version does not take place it can be assumed that either there is very little liquor, or that the limbs are extended. If facilities are available this last point is easily checked.

When performing external version, the conditions *in utero* must be kept in mind. The emphasis should be laid on inducing the foetus to undo its extension, and to turn rather than on the attempt to force around an inanimate object of the wrong shape. The foetus will respond to stimuli as Barcroft¹³ and others have shown. Gentle pressure on the cephalic end will nearly always induce vigorous movements. This may well undo the extended attitude, and the foetus, "taken unawares," may be moved around partly or wholly. The foetus should be taken around the way of least resistance. There is no need to fear causing the extended attitude; that is there already. As the foetus is most responsive to pressure on its facial aspect, turning it backwards is often successful when forward or orthodox version fails and was advocated by Spencer¹⁴ in 1901 though based on an experience of only 6 cases. Only one pole should be pressed upon at a

time to allow the foetus to bulge out the uterus at the other. The operation must never be so violent as to distress either mother or foetus, and it can be repeated every week or oftener if it is thought necessary, until the final decision is reached.

Anaesthesia is unlikely to help in most cases. Patients are taught the virtues of relaxation antenatally as a preparation for their labour, and much better relaxation can be achieved with a patient's intelligent co-operation than will be obtained with anything short of deep anaesthesia. When this deep anaesthesia has been obtained, the temptation to overcome the obstinacy of the foetus is too great for many to resist; and that way lies disaster. Wrigley¹⁵ gives the appalling infant mortality figure of 13 per cent after external version under anaesthesia. In this series it was only employed when the patient was intolerant of any attempt being made without. It was used 9 times in 392 attempted versions. No foetal death occurred.

Antepartum haemorrhage (accidental) occurred twice. Once very slightly at the time of a version under anaesthetic; once a fairly considerable loss occurred in a patient who had had an external version 10 days previously without an anaesthetic.

If the breech delivery is conducted by an experienced obstetrician or midwife, then the mortality does not seem to be any higher than in the case of the vertex. The breeches which are lost by the experienced are often cases of dystocia. Breech foetal survival should be compared with the survival rates of the vertex in dystocia if a correct sense of proportion is to be maintained.

It is when difficult delivery is added to the unusual presentation, that the mortality begins to go up. It is incumbent therefore on the obstetric team to see that no woman who has a persistent breech shall also be asked to deliver herself of a large baby

which we also know from experience will in the great majority of cases be in the extended attitude.

If the baby seems large or the pelvis small, then failure to eliminate the breech by the 38th week, is strong indication for the induction of premature labour, or, if it is held that even then the foetus is too large for comfort, the indication is for planned Caesarean section at term.

This plan has been followed in this series. Of the 38 persistent failed versions, 4 were medically induced, and 11 surgically by the rupture of the membranes. One Caesarean section was performed. In the remaining 22 the size of the foetus, and the capacity of the pelvis were correctly judged to allow of a good prognosis being given and no interference was necessary. Seven pounds, 13 ounces in a primigravida, and 8 pounds 14 ounces in a multigravida, were the heaviest babies born as a breech.

The weight groups were as follows:

| Pounds | Pounds | Pounds | Pounds | Pounds |
|--------|--------|--------|--------|--------|
| 3 to 4 | 4 to 5 | 5 to 6 | 6 to 7 | 7 to 8 |
| 1 | 0 | 4 | 18 | 10 |

The deliveries were conducted by the rotation method described by Løvset¹⁶ of Bergen, and in most cases the forceps was applied to the after-coming head.

THE SKIAGRAMS.

Examination of the drawing of the skiagrams shows that when the foetus eventually turns the attitude is for the most part flexion or semi-flexion, whereas when the foetus resists version the attitude is most often extension. The quantity of liquor in the uterus can also be gauged by the stance of the foetus.

It is also seen, however, that it is not possible to say from the examination of a

photograph, what will happen, but only what is most likely to occur.

SUMMARY.

By way of summarizing, I return to my nine postulates.

Breech presentation in pregnancy is so common that at the appropriate stage it is normal. It is the persistence beyond this stage that constitutes the abnormality.

In 60 per cent of cases spontaneous version will take place.

Once it has taken place reversion only very seldom takes place.

Version is shown to be most often completed by the 32nd week.

External version as a therapeutic measure is therefore indicated for the breech persisting after the 32nd week.

Failed version usually means little liquor and an extended attitude.

These two factors therefore stand out as the real aetiological factors of breech presentation at term.

Multiparity and prematurity are also factors.

The clinical work upon which this paper is based was done at The British Hospital for Mothers and Babies at Woolwich.

In January 1941, when the maternity department at the Memorial Hospital, Woolwich, was shut down, I asked permission to see antenatal cases at this hospital. Not only was permission graciously given by Miss Gregory and Miss Cashmore, but the utmost assistance was afforded to me by the staff there, all very experienced midwives, among whom I would particularly thank Sister Nield, and Sister Grose for the help they have given me. I have been able to use the observations made by

the other physicians; their notes were an indispensable supplement to my own, and I am very grateful to them for their assistance.

Dr. Eileen Wise was in charge of most of the deliveries. The fact that the only babies which were lost in this series were 5 macerated, 6 premature, and 1 abnormal foetus, is a tribute to her obstetric skill, and I record my profound admiration for it.

I am also grateful to Professor Browne for reading through this paper prior to its publication and for his helpful criticism.

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Body Temperature—A Diagnostic Aid in Menstrual Disorders and Sterility

BY

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AS early as 1904 Van der Velde¹ discussed the variations in body temperature which occur during the menstrual cycle. In the last few years additional evidence of the diagnostic value of body temperature graphs has accumulated.

Palmer² made observations on 35 normally menstruating women during 130 complete cycles. The temperature graphs showed usually a constant biphasic curve with a relatively constant luteal phase, independent of the length of the cycle. The patients took the rectal temperature every morning on awakening. In no case observed was there any discrepancy between the phase of the cycle as indicated by the basal body temperature curve and the endometrial specimens. The following observations were made:

Secondary amenorrhoea due to persistent follicular activity (as confirmed by endometrial biopsy). Basal body temperature persistently low.

Secondary amenorrhoea due to primary pituitary dysfunction. Basal body temperature higher without fluctuations (similar to the type seen in menopausal women).

Oligomenorrhoea ($1\frac{1}{2}$ to 6 months cycles): Basal body temperature showed a constant rise 14 days before menstruation.

Onset of pregnancy: Basal body temperature showed sustained temperature elevation.

Martin³ had 99 patients taking the vaginal or rectal temperature during 181 cycles. The temperature graphs of normal men-

struating women showed a constant biphasic curve with a constant luteal phase. Fluctuations of temperature occurred between 0.3°F. and 1°F. with the following changes during the menstrual cycle:

Premenstrual phase. Fall of temperature.

Menstrual phase. Low temperature.

Oestrogenic phase. Low temperature.

Ovulatory phase. Sudden rise of temperature.

Luteal phase. Sustained elevation of temperature.

He observed that injections of oestrogen lowered the basal body temperature, whereas injections of progesterone raised the basal body temperature.

Williams⁴ investigated the basal body temperature of 35 women during 2 months, in correlation with their basal metabolic rate and found temperature variations during the cycle to be between 0.9°F. and 1.6°F. with a low point of temperature on the day of ovulation. He could not detect any correlation between basal body temperature and basal metabolic rate.

Lyon⁵ investigated the basal body temperature in cases of functional dysmenorrhoea during 127 cycles in 30 females aged 16 to 34 years, and noted the characteristic rise in the temperature curve preceding each flow when pain occurred. When occasionally the temperature curve lacked the premenstrual rise, and thus labelled a cycle as non-ovulatory, dysmenorrhoea did not occur in that cycle. Lyon con-

cludes that a progestational endometrium is necessary for the typical cramps of functional dysmenorrhoea, and that the basal temperature curve can be of help in differentiating functional dysmenorrhoea from other kinds of menstrual pain.

Tompkins⁶ corroborates the findings of others and reports coitus or artificial insemination leading to successful pregnancies when practised on the sudden rise of temperature after its previous low drop during the midcycle.

INVESTIGATION OF VAGINAL AND ORAL TEMPERATURE CURVES IN 41 WOMEN DURING 150 CYCLES.

Experimental Procedure.

The 41 women comprised subjects with normal cycles, menopausal patients, and

patients suffering from various forms of primary and secondary amenorrhoea, menorrhagia, intermenstrual bleeding and dysmenorrhoea. The effects of oestrogen, progesterone, androgen and vitamin B administration on the temperature curve were investigated. All women took vaginal, oral or both temperatures simultaneously every day at the same time, usually in the evening.

Results.

Women with normal cycle (Fig. 1). Twenty-three cycles were investigated.

Premenstrual phase. Fall of temperature about 1 or 2 days before menses.

Menstrual phase. Further decrease of temperature which may reach a level as low as 97°F. followed by a rise to about 98°F. or 99°F.

Fig.1

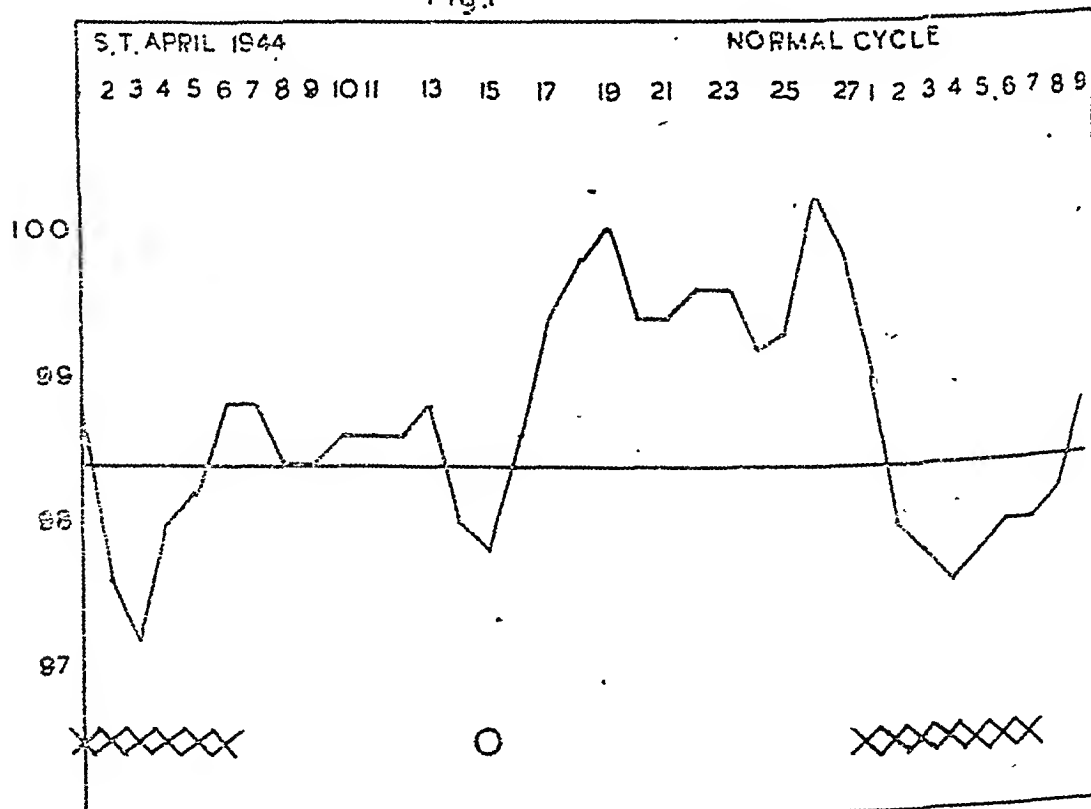
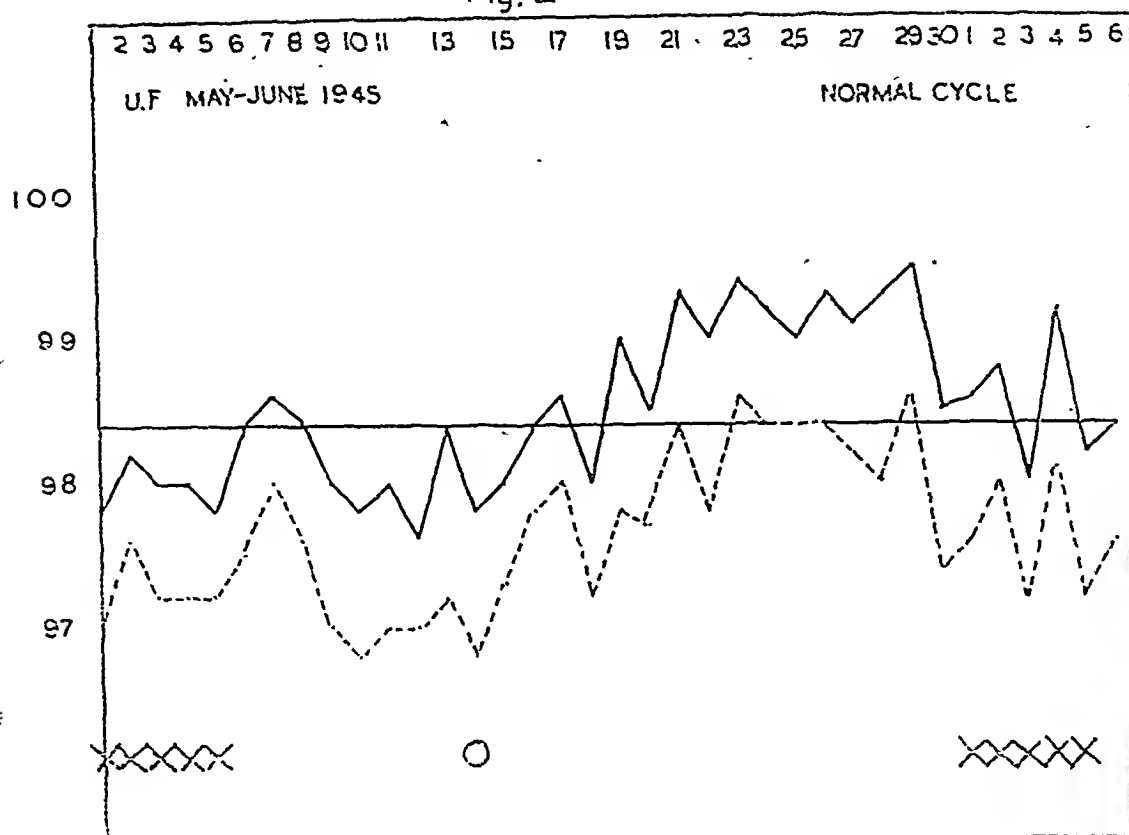


Fig. 2



Follicular phase. This phase is characterized by a low fluctuating temperature of approximately 98.4°F. to 99°F.

Ovulatory phase. In normal women a sudden fall of temperature usually occurs on the 14th day before the onset of menses. It sometimes reaches a point as low as 97°F. followed by a sudden rise.

Luteal phase. A sustained elevation of temperature reaching 100°F. or higher, continuing until about 1 or 2 days before the menses.

Mid-luteal phase. A slight decrease of temperature takes place at this phase, corresponding with the oestrogenic peak.

Oral and Vaginal Temperature.

Thirty-four cycles have been observed of patients taking oral and vaginal temperatures simultaneously, and these temperature curves in all cases show an almost identical pattern. Rise and fall of vaginal temperature is almost always accompanied by a rise and fall in oral temperature. The follicular, ovulatory and luteal phases are well expressed by the oral temperature (Fig. 2). In the normal woman the difference between oral and vaginal temperature taken in the evening is about 0.6°F. to 0.12°F. (Fig. 2). This difference may decrease or increase, or disappear completely in various forms of genital hypoplasia (Fig. 3). The curves of morning

temperature differ from those taken in the evening, particularly when the patient is given treatment which elicits temperature changes (Fig. 4).

Although the temperature curves are of the same pattern, the oral and vaginal temperatures react differently to oestrogen and progestin. Each of the hormones acts individually, producing curves of different height, a fact which greatly facilitates the diagnosis of functional disorders.

Progestin in Presence of Oestrogen.

Observation of vaginal and oral temperature curves (both temperatures taken simultaneously) throughout many cycles has revealed that progestin administration in the presence of oestrogen produces

a greater increase of vaginal than of oral temperature. Although both oral and vaginal temperature curves rise, the distance between the curves increases (Fig. 5.)

Oestrogen.

The administration of oestrogen, on the other hand, produces a greater decrease in oral than in vaginal temperature (Figs. 6 and 7). Thus, both progestin in presence of oestrogen, and oestrogen increase the distance between the oral and vaginal curves.

Progestogen in Oestrogen Deficiency.

Administration of progestogen in the absence or relative deficiency of oestrogen,

Fig. 3

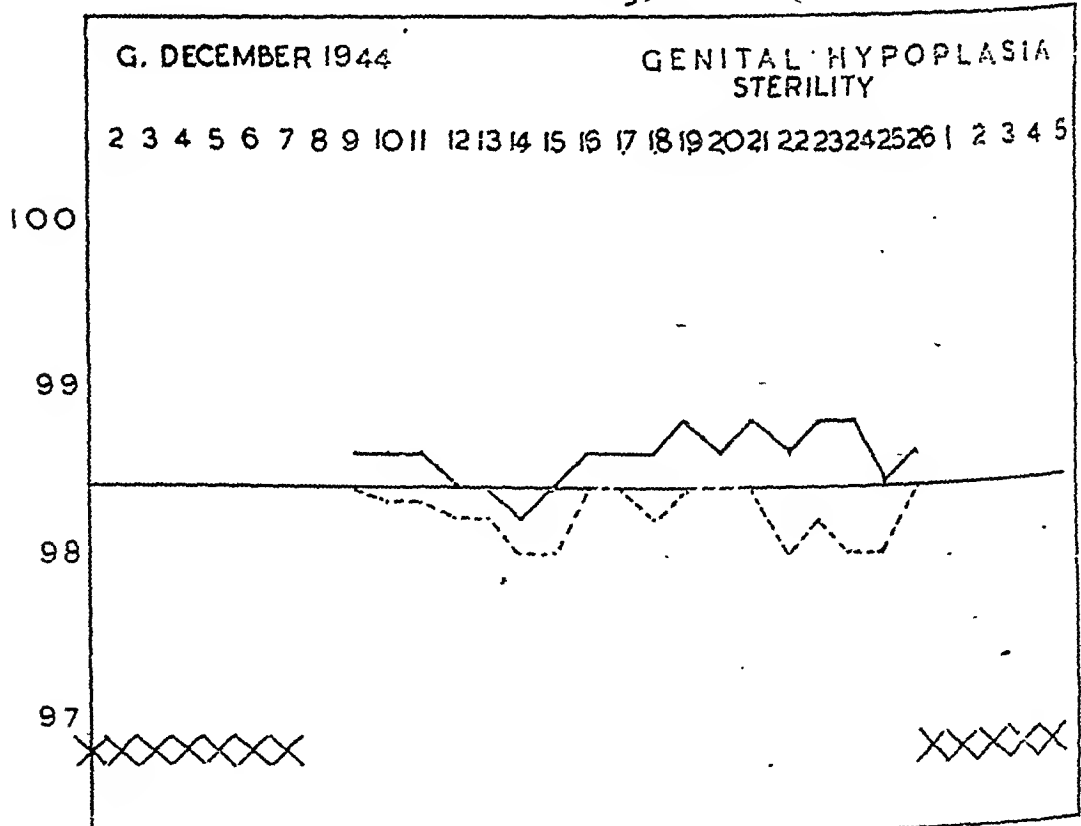


Fig.4

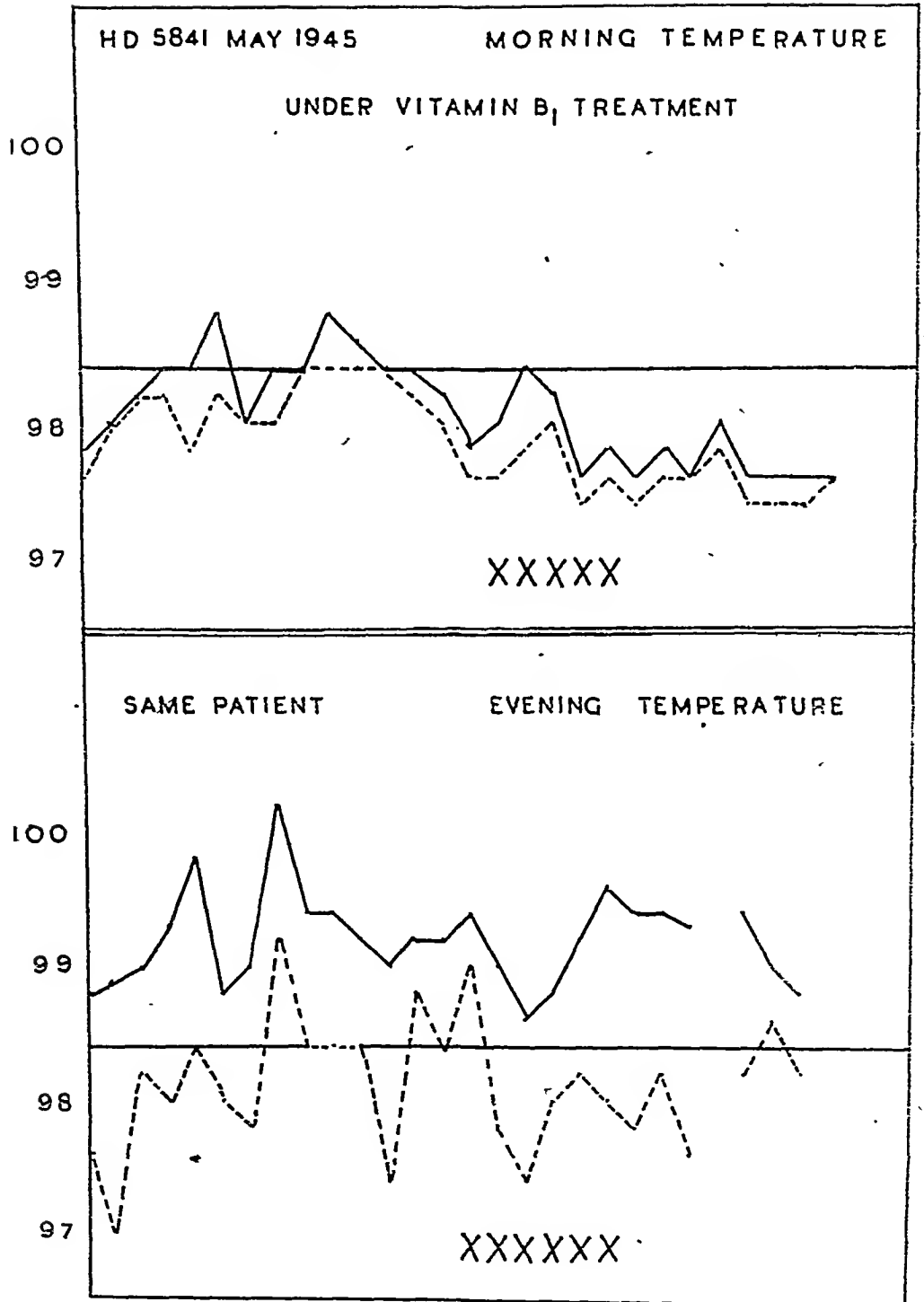
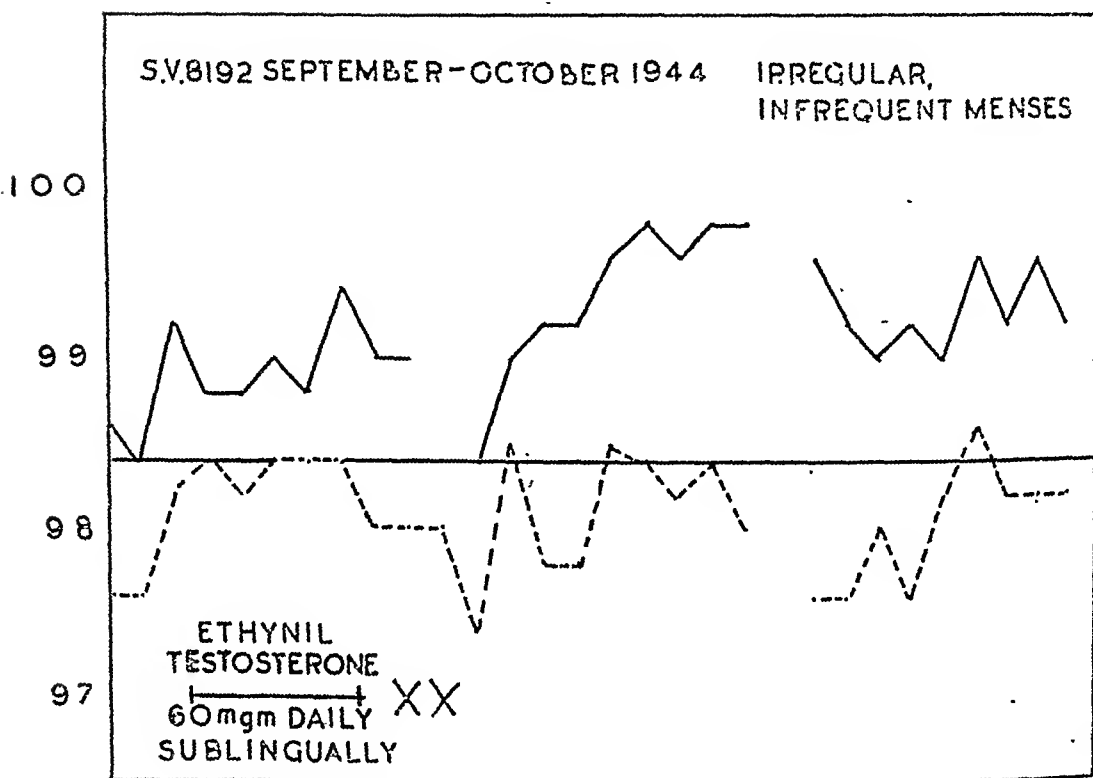


Fig.5



has a greater effect on the oral than on the vaginal increase of temperature, causing an approximation of the curves (Fig. 7). The oral curve, free from the temperature lowering action of oestrogen, rises at a relatively greater rate towards the level of the vaginal curve. The oral curve rises proportionately to the relative or absolute state of oestrogen-deficiency, and may reach the level of the vaginal curve and be separated only after renewed oestrogenic activity occurs, or progestin withdrawal takes place (Figs. 6 and 8).

Both progestogen and oestrogen increase the distance of the temperature curves, progestogen with predominant action on the vaginal temperature, and oestrogen dominating the oral temperature.

Secondary Amenorrhoea.

The temperature in cases of secondary amenorrhoea due to protracted follicular activity, either of polyfollicular or hyperfollicular nature, shows a persistently low curve, either fluctuating or constant (Figs. 11 and 12). It is tempting to associate the constant low temperature with hyperfollicular amenorrhoea and the fluctuating low temperature with polyfollicular amenorrhoea. A higher temperature curve frequently observed in secondary amenorrhoea, is presumably due to pituitary failure or persistent luteal activity, or both (Fig. 10).

Oligomenorrhoea.

The follicular phase is prolonged and

menses occurs 14 or more days after ovulation (Fig. 8).

Menorrhagia.

There is constantly a prolonged follicular phase with delayed ovulation and short luteal phase (Figs. 11 and 15).

The temperature, however, does not fall as normally in the premenstrual phase, but remains on a high level until the end of the menstrual phase.

Dysmenorrhoea.

Thirty-eight cycles were examined and all showed a lack of the normal oestrogenic fall of temperature one or two days before onset of menses. On the contrary,

a rise of temperature occurs which decreases only at the end of menstruation or after menstruation has ceased (Figs. 6, 8, 14, 15 and 16).

Patients taking both oral and vaginal temperatures show a rise of both curves prior to menstruation.

The oral temperature, however, increases at a greater rate than the vaginal, approaching and finally reaching the level of the vaginal curve before or during menses. Renewed oestrogenic activity lowers both curves with predominant action on the oral temperature so that the distance between the curves again increases (Figs. 6 and 8).

Fig. 6

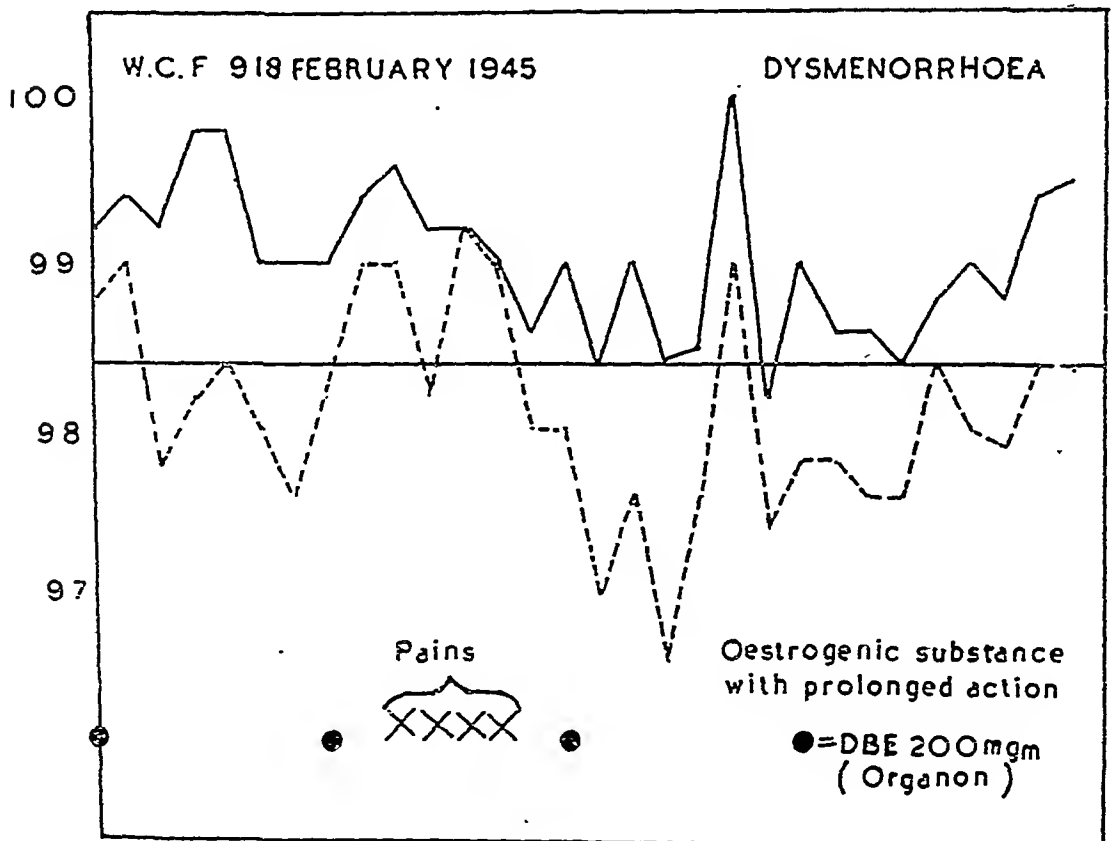
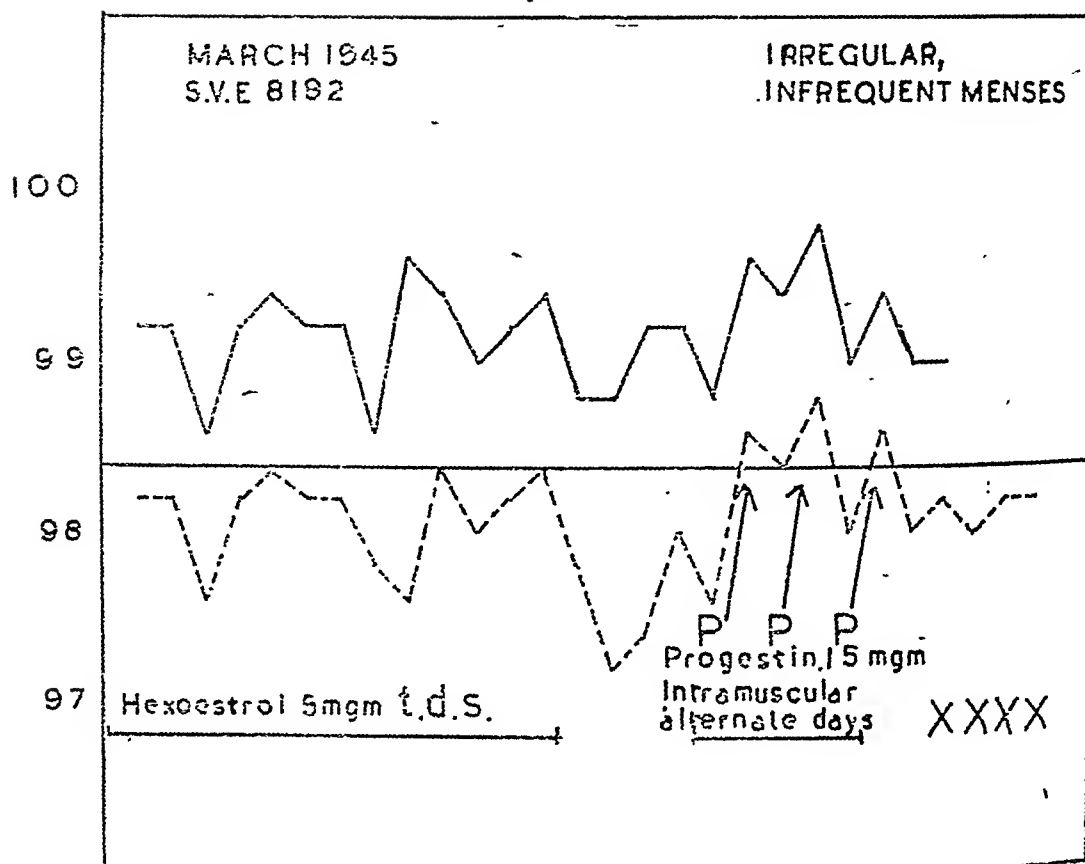


Fig. 7'



An exacerbation of pain was noted in those cycles in which such approximation or union of the curves occurred (Figs. 6 and 8).

Intermenstrual Bleeding.

Patients suffering from intermenstrual bleeding show a relatively high temperature curve with only minor fluctuations. Bleeding each time is associated with only slight increase in temperature (Fig. 17).

Menopause.

The temperature during the menopause may be either high or low, and always shows a constant pattern or with very slight fluctuations (Fig. 18).

Oestrogen Administration.

Administration of oestrogen always produces a lowering of temperature, frequently producing a characteristic curve of marked up-and-down fluctuations of 1°F. and more (Figs. 19 and 20).

It is interesting to note that this characteristic curve of marked up-and-down fluctuation in some cycles occurs about 12 days after the beginning of oestrogen administration, lasting about 12 to 14 days. In other cycles it may start 12 to 14 days followed by a sustained rise of temperature.

Oestradiol benzoate 60,000 units intramuscularly injected in 3 doses of 20,000 I.B.U. over 2½ hours into a menopausal woman produced a decrease of temperature

Fig. 8

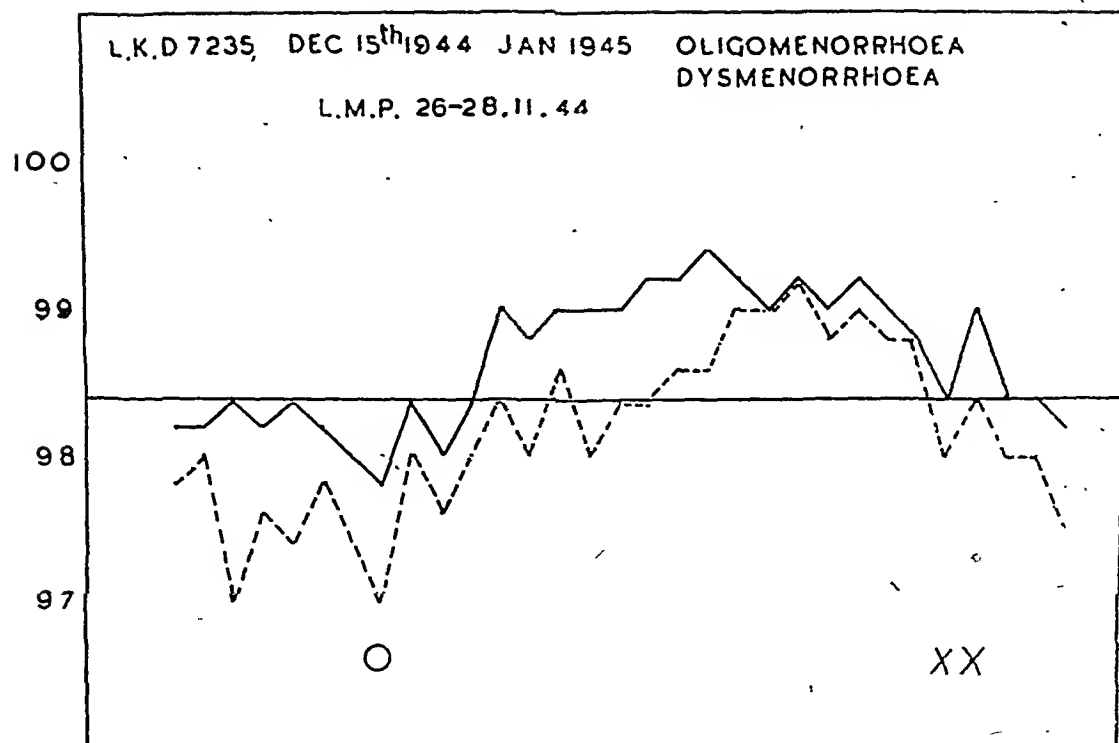
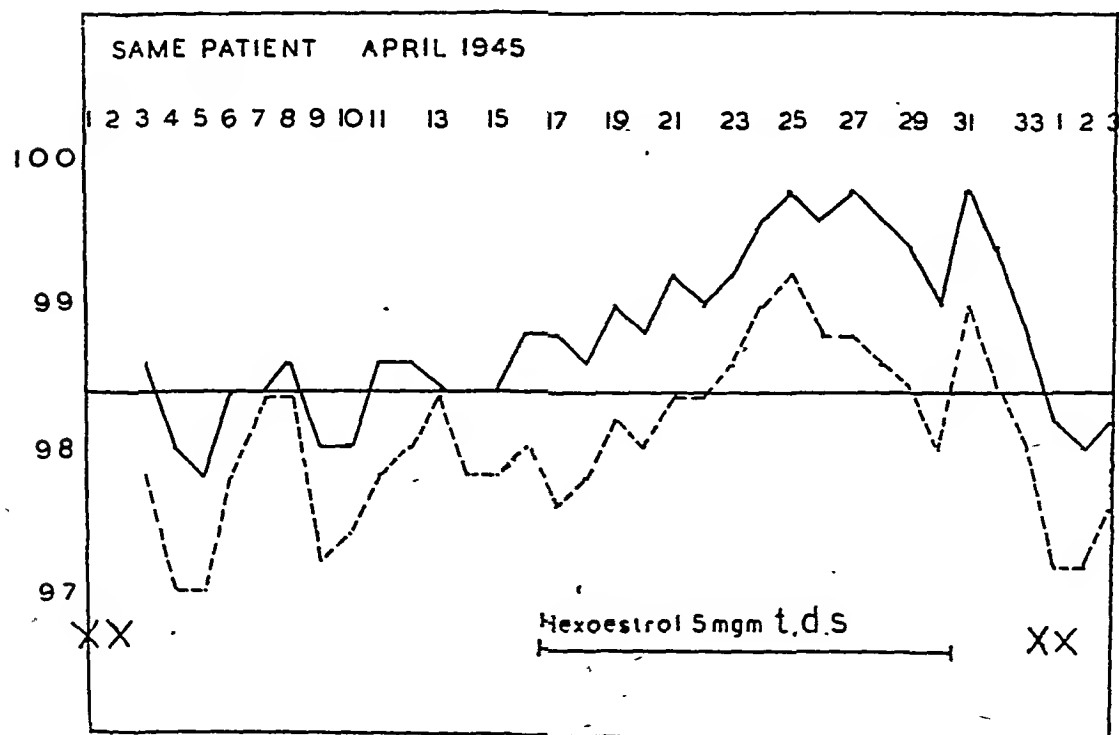


Fig. 9



by 2°F. within 4 hours after the last injection, and remained at this level for 7½ hours (Fig. 21).

Progesterone 2 c.cm. (2 mg.) intramuscularly stopped the beginning rise of temperature and kept it at a low level for a further 3 hours, probably by protecting oestrogen against its inactivation, Pincus and Zahl.⁷ The temperature then returned to the pre-injection level, proceeding however, with marked fluctuations (Fig. 22).

Progestogen Administration.

Administration of ethynil testosterone in the dosage of 60 mg. daily sublingually for 5 days to patients suffering from secondary amenorrhoea due to protracted follicular activity (either hypo- or poly-follicular) causes constantly a marked even rise of temperature and onset of bleeding about

2 days after cessation of treatment (Figs. 11, 22 and 23).

If progestogen is given together with oestrogens as, for instance, Lutocyclin 15 mg. with oestradiol benzoate 25,000 I.B.U. in one syringe intramuscularly in 3 doses on alternate days, it causes only very slight increase of temperature followed on the 3rd or 4th day after cessation of treatment by menses of normal length and flow (Fig. 24).

Androgen Administration.

Administration of testosterone propionate or methyl testosterone in small doses expresses itself in a decrease of temperature if given during the follicular phase (Figs. 14 and 15). This is in accord with the findings of Selye and others⁸ that androgens in small doses have folliculoid activity. The

Fig.10

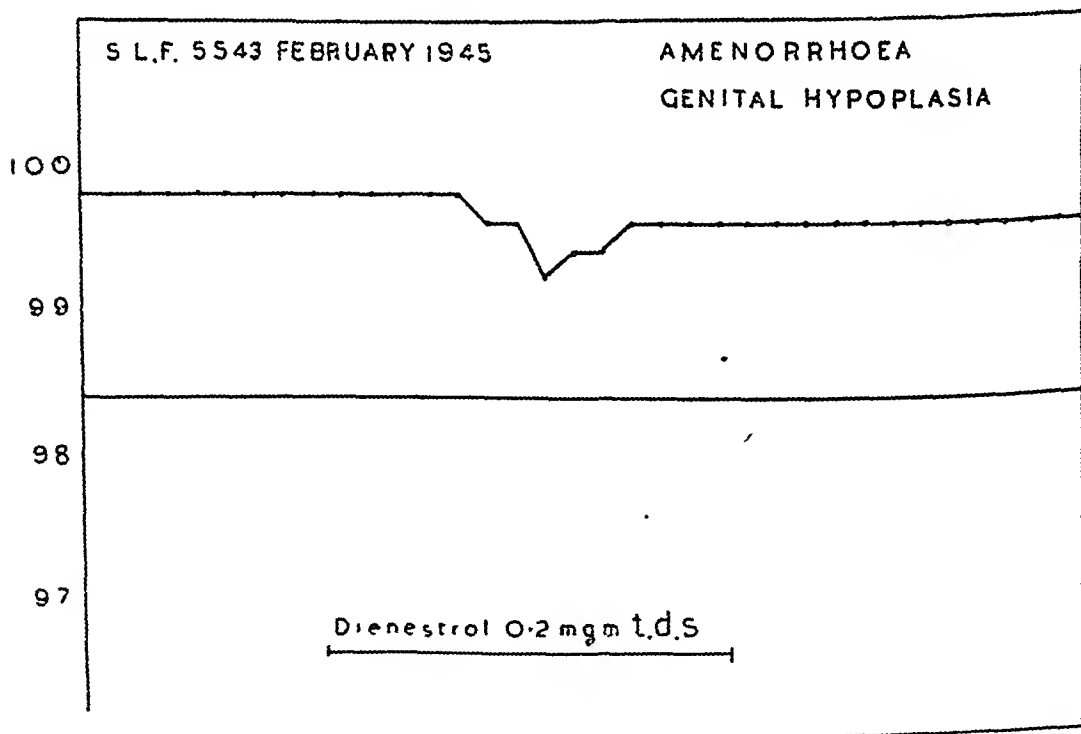


Fig.11

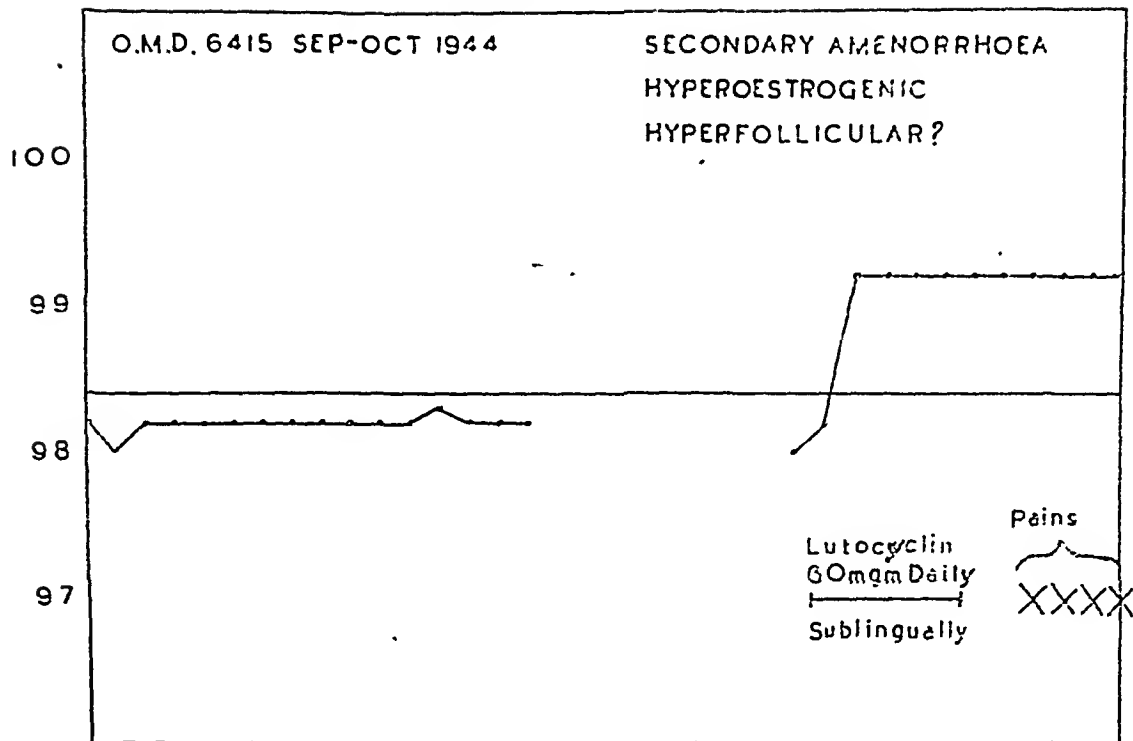


Fig.12

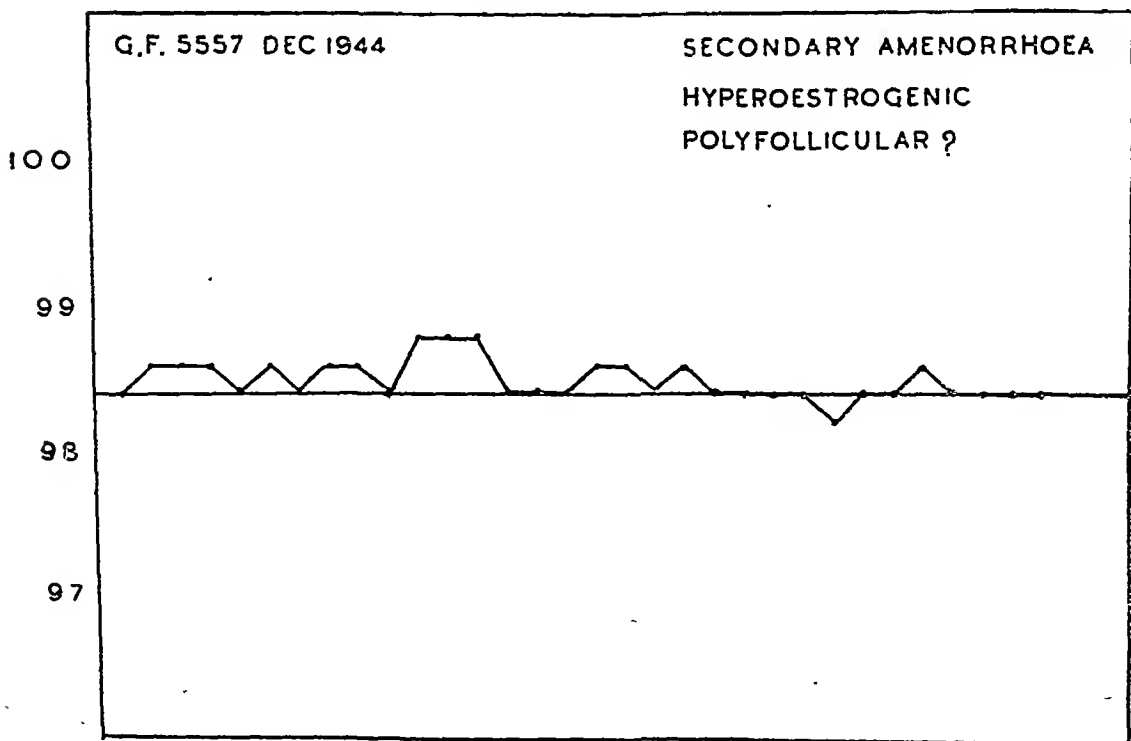
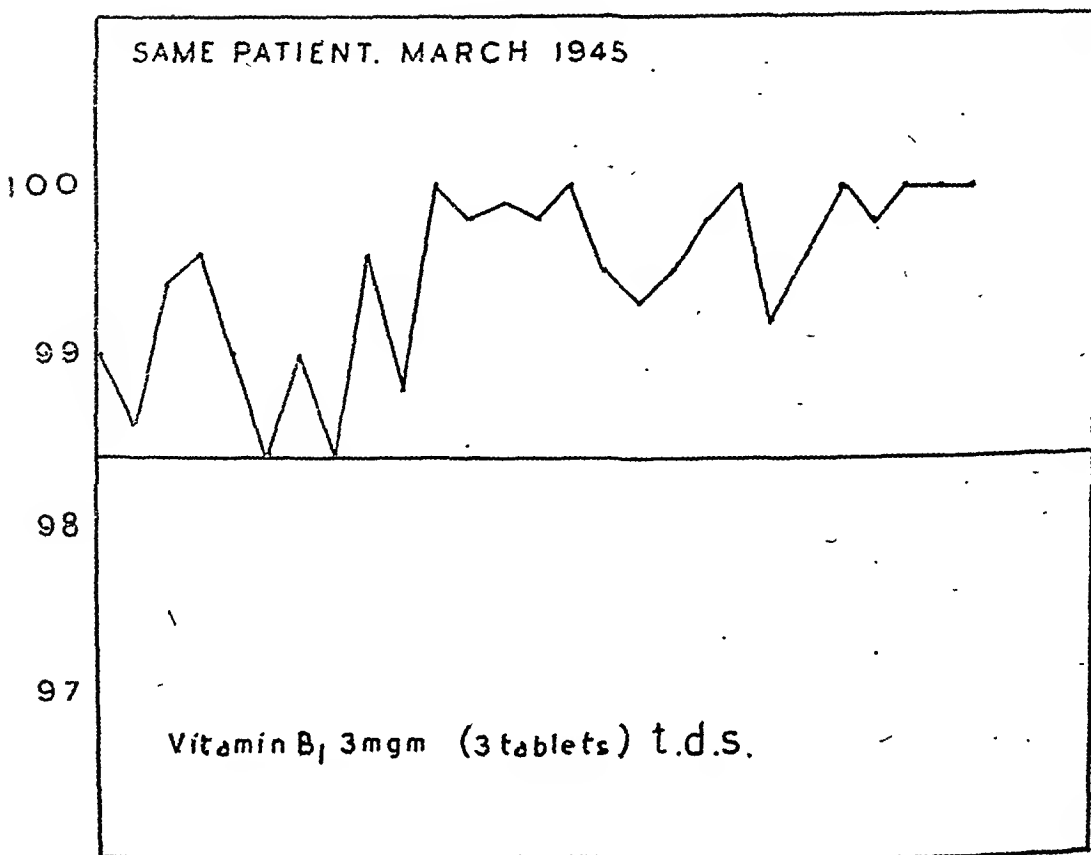


Fig.13



beneficial effects of androgens in the treatment of menorrhagia, metrorrhagia and polymenorrhoea may be due, not to its constricting effect of the myometrial spiral arterioles as hitherto believed, but to its folliculoid action.

Vitamin B Administration.

Vitamin B administration to patients with high oestrogenic level due to protracted follicular activity causes a marked increase of temperature (Figs. 12 and 13). This fact is in accord with Biskind and others⁹ who found that vitamin B increased the inactivation of oestrogen in the liver.

DISCUSSION.

The temperature variations during the menstrual cycle closely correspond to changes in glandular activity, particularly of the pituitary gonadotrophic, follicular and luteal hormones. It is suggested that the decrease of temperature is an expression of oestrogen activity, whereas temperature rise is caused by the corpus luteum hormone.

Premenstrual Phase.

The fall of temperature during the premenstrual phase is due to corpus luteum

Fig.14

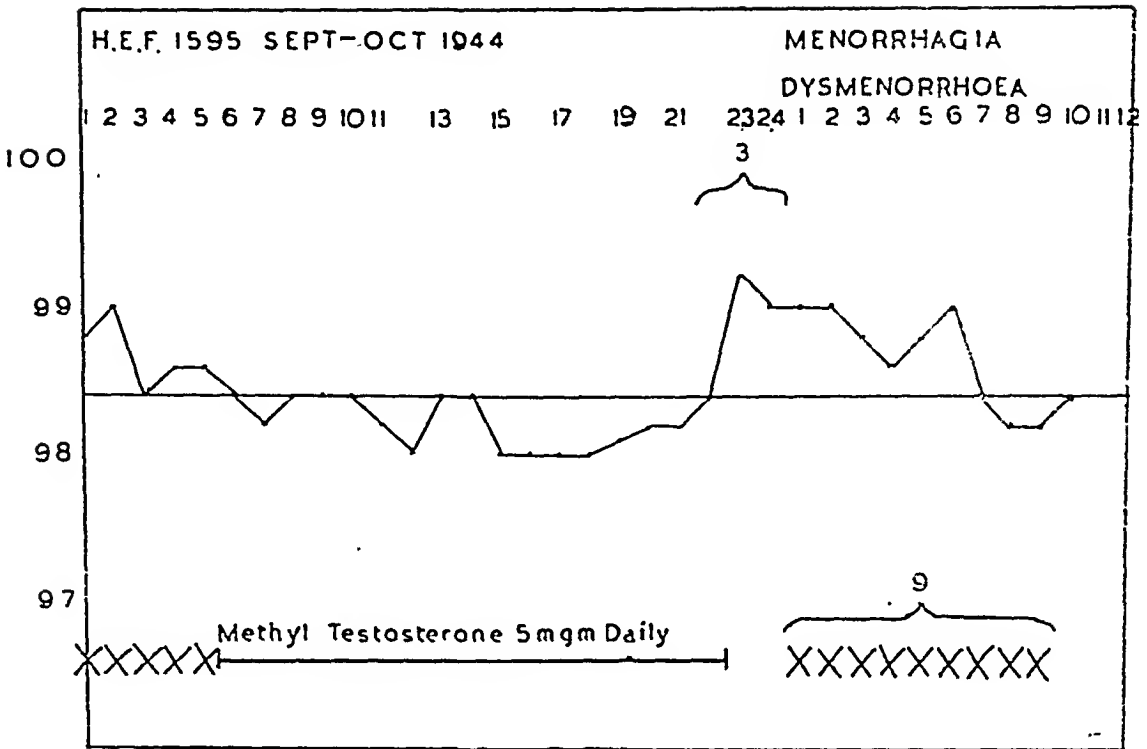
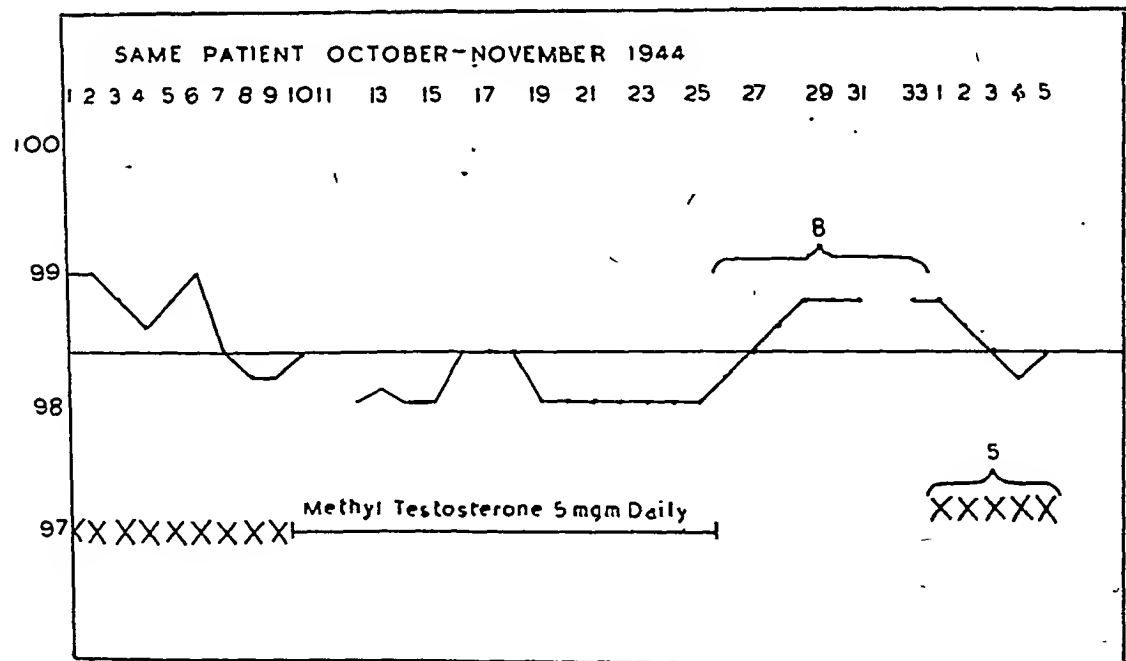


Fig.15



regression and renewed oestrogen excretion.

Oestrogenic activity is preceded by oestrogen and progestin withdrawal and coincides with the release of follicle-stimulating hormone of the anterior pituitary and formation of new follicles.

Menstrual Phase.

During the menstrual phase the temperature continues to decrease, owing to the still very vigorous release of F.S.H. which causes a high rate of follicle maturation. Increased oestrogenic activity inhibits the excretion of F.S.H. from the pituitary and decreases the rate of follicle maturation, which results in a diminished oestrogen excretion. This corresponds to the subsequent rise of temperature during the menstrual phase.

Follicular Phase.

The sustained low fluctuating temperature during the follicular phase corresponds to a more or less even rate of follicle maturation and oestrogen excretion.

Ovulatory Phase.

Usually, on the 14th day before menstruation, oestrogen excretion reaches its highest peak causing the sudden drop in temperature. This is followed by vigorous release of luteinizing hormone from the anterior pituitary which produces ovulation and corpus luteum formation with increased progestin excretion.

Luteal Phase.

At this stage the temperature rises to a level between 99°F. and 100°F. or more,

Fig.16

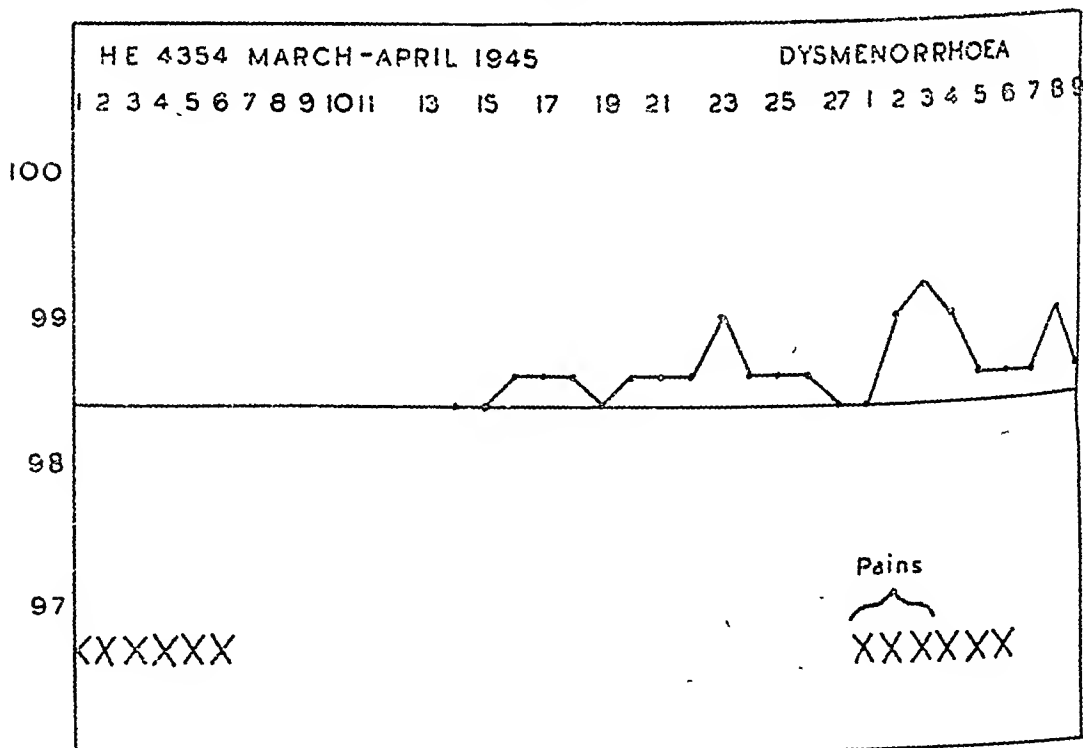
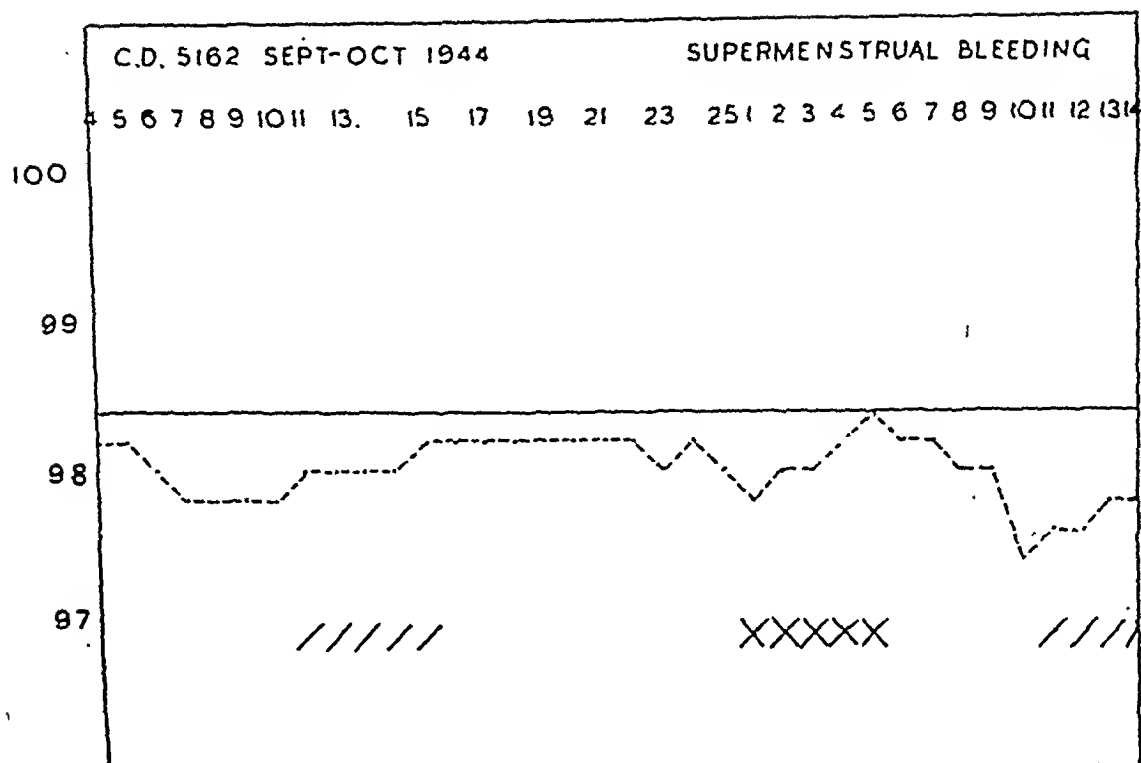


Fig. 17



and remains at this level with slight fluctuations throughout the whole luteal phase. It declines 1 or 2 days before onset of menses.

Mid-luteal Phase.

The slight decrease of temperature is caused by the oestrogenic peak occurring at this stage of the phase.

The difference between the lowest temperature in the follicular phase and the highest temperature in the luteal phase is, in the normal woman, approximately 1.4°F. It is interesting to note that this difference is less obvious with the increased grade of genital hypoplasia (Fig. 3).

Secondary Amenorrhoea.

Two kinds of secondary amenorrhoea have been included in the classification of

temperature curves, one characterized by persistently low temperature, and the other associated with a higher temperature curve (Figs. 10, 11 and 12).

The patients presenting a low curve showed normal genital development frequently associated with a tendency to obesity. Neither protracted nor cyclic oestrogenic treatment is of any avail in producing oestrogen withdrawal bleeding in these patients.

In the author's experience ethynil testosterone 60 mg. sublingually daily for 5 days always produced bleeding on the 2nd or 3rd day after cessation of treatment in patients suffering from hyper-oestrogenic amenorrhoea due to protracted hyper- or poly-follicular activity (Figs. 11 and 23). Such patients who, in addition, suffered

from obesity showed a loss of weight under continued treatment. Progestogen administration to these patients is always accompanied by a rise of temperature.

The persistent state of amenorrhoea in untreated patients with a high oestrogenic level may be due to the fact that the hormone is constantly above the endometrial sub-threshold bleeding point, and adequate to maintain the proliferated mucosa without causing endometrial breakdown and bleeding.

It is doubtful whether an upper bleeding threshold exists in view of the fact that most cases of amenorrhoea treated by oestrogen withdrawal showed by their

vaginal temperature curves, either signs of pituitary or direct¹⁰ ovarian stimulation (Figs. 10, 20, 25, 26, 27 and 28), or sub-threshold oestrogen withdrawal bleeding (Figs. 9, 25 and 27).

It seems more justifiable to speak of menses accompanied by a high oestrogenic level as in the case of normal menses which, although preceded by oestrogen withdrawal, is usually associated with a high oestrogenic level.

Low oestrogenic bleeding, on the other hand, occurs in cases of menorrhagia, metrorrhagia and intermenstrual bleeding (Figs. 14, 15, 16 and 24), is usually of protracted nature and is easily suppressed by

Fig.18

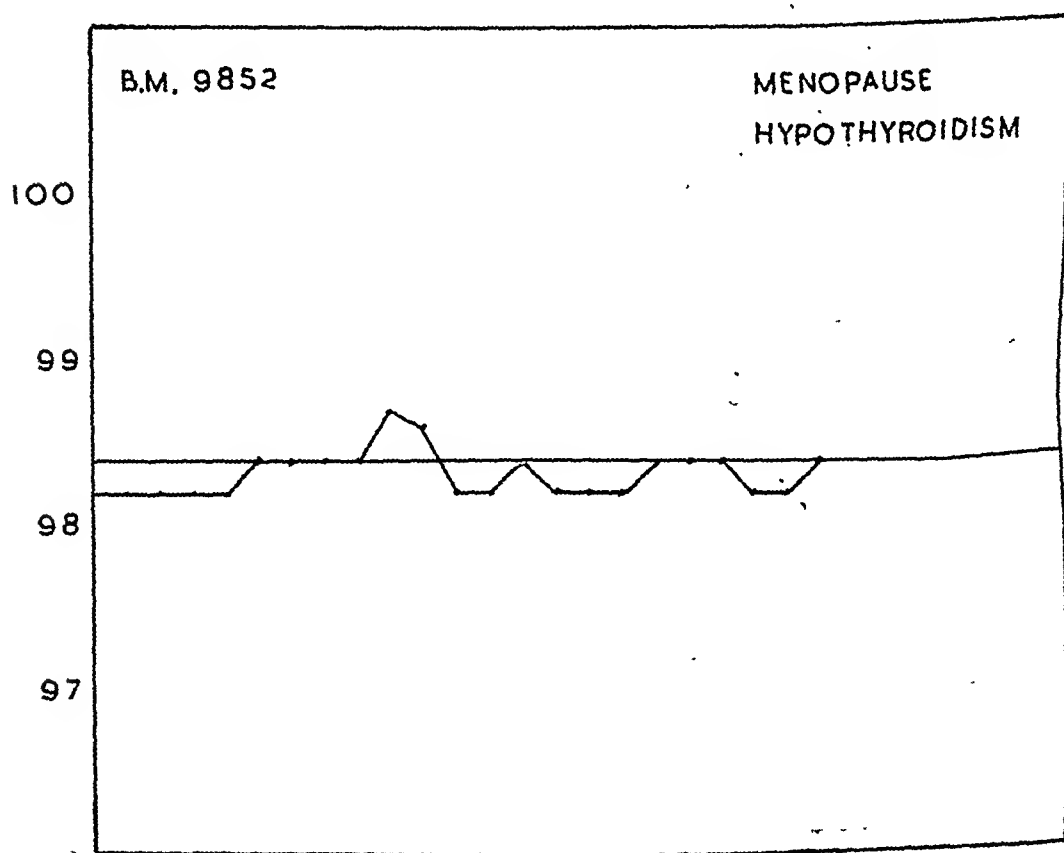
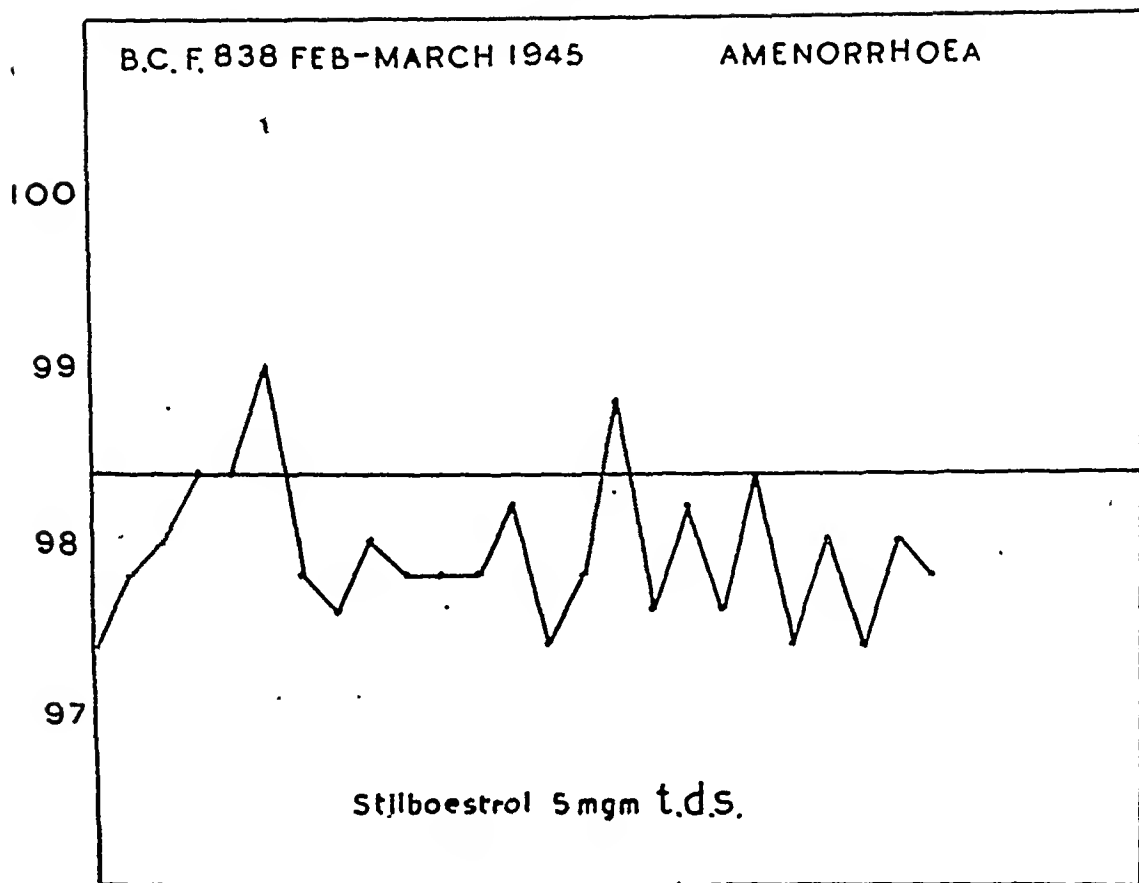


Fig. 19



raising the oestrogenic level. One injection of oestradiol benzoate 100,000 I.B.U. intramuscularly usually stops bleeding within 24 hours.

A low constant temperature curve seems to be associated with hyperfollicular amenorrhoea, whereas the low curve with slight fluctuations may be a sign of polyfollicular amenorrhoea. The latter is usually of shorter duration (Fig. 12).

The constant high temperature curve denoting oestrogen deficiency is usually found in patients with signs of genital hypoplasia (Fig. 10).

In cases of a vaginal evening temperature curve above the level of 98.8°F. (Fig. 29)

the treatment of choice is cyclic oestrogen-progestogen administration (Fig. 7).

At values below 98.8°F. denoting a somewhat higher oestrogenic level sole oestrogen withdrawal treatment may suffice (Figs. 27, 28 and 29).

As the oestrogenic level increases the administration of the hormone may remain without effect, and the treatment of choice in these cases is progesterone 15 mg., and oestradiol benzoate 25,000 I.B.U. in one syringe intramuscularly alternate days in 3 doses. Menses of normal length and flow usually follow on the 3rd or 4th day after cessation of treatment (Figs. 29 and 24).

Still higher levels of oestrogen require only progestogen treatment in the form of ethynil testosterone 60 mg. sublingually daily for 5 days or progesterone 15 mg. intramuscularly for 3 days (Figs. 11 and 23).

An initial success may sometimes be obtained with progestogen at high temperature levels, while subsequent administration acting on a previously reduced oestrogenic level will remain without results.

The temperature values are only approximate and should be regarded as such when, in accordance with temperature level, the particular treatment is decided upon.

Oligomenorrhoea.

Infrequent bleeding from a secretory type of endometrium has revealed temperature graphs showing a variable prolonged follicular phase with a fairly constant luteal phase. Menses occurs 14 days or more after ovulation (Fig. 8).

There is as yet no evidence at hand why ovulation is delayed in these cases.

Repeated observations made on the basis of endometrial biopsies are conflicting as to whether oligomenorrhoea is caused by a prolonged follicular phase or protracted luteal phase.

Too few cases of oligomenorrhoea have been investigated by their temperature to allow the support of one or other opinion.

Infrequent bleeding from non-pregesta-

Fig.20

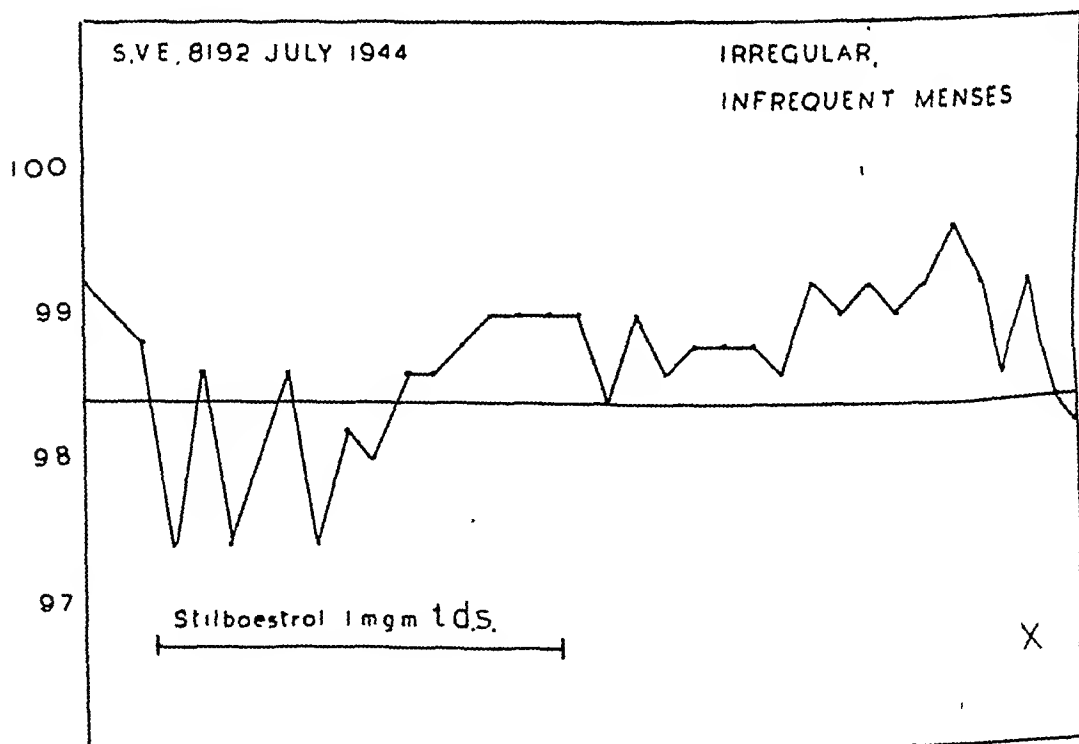
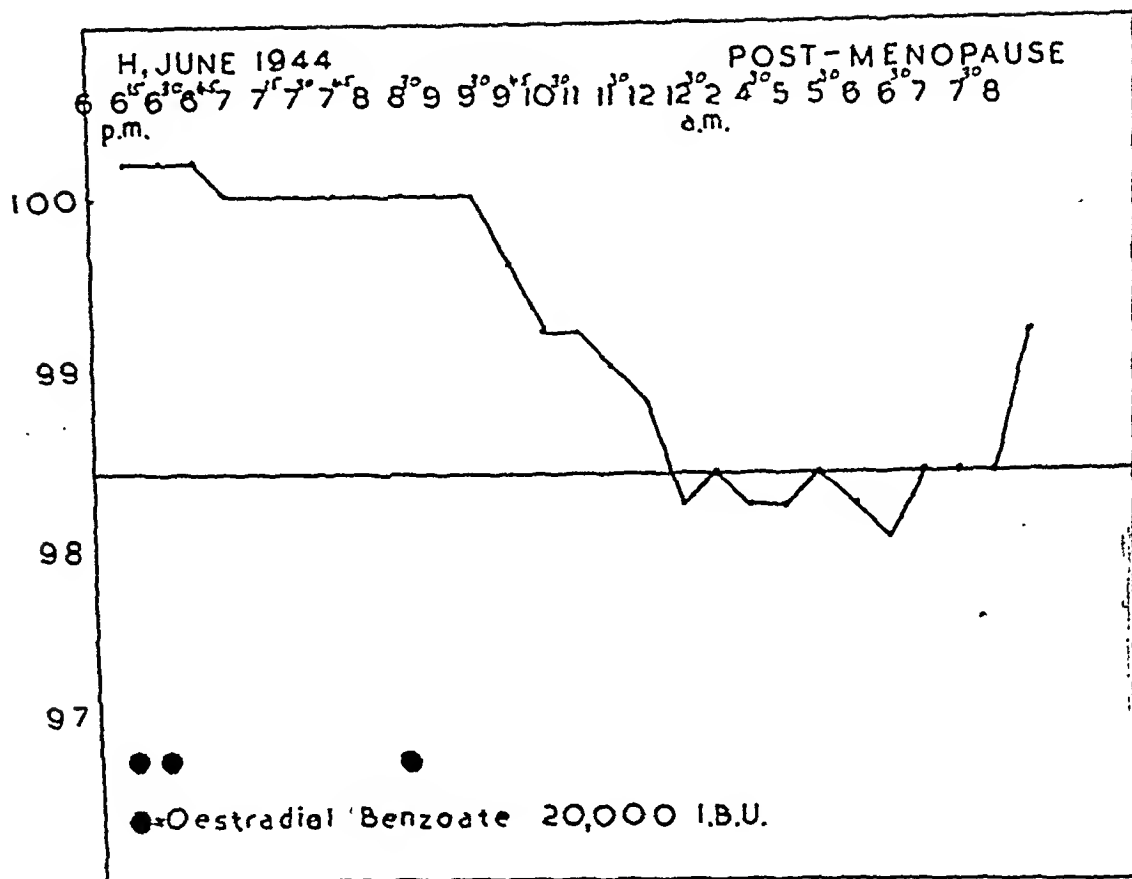


Fig. 21



tional endometria is classified under secondary amenorrhoea.

Menorrhagia.

The temperature curves in cases of menorrhagia show a prolonged follicular and short luteal phase. Bleeding occurs in short distance of ovulation and is characterized by a lack of the premenstrual phase in which normally the temperature falls (Figs. 14 and 15).

During the menstrual phase the temperature remains at a high level and falls at the end or after the menstrual phase. In fact, however, the follicular and luteal phases are approximately of the same and normal

length, but bleeding occurs before corpus luteum regression has taken place. This is in keeping with the observations of Traut and Kuder,¹¹ in whose opinion menorrhagia occurs from endometria which show evidence of deficient luteal influence. Conversion to the secretory phase occurs only in scattered areas.

Further supporting evidence is supplied by Samuels¹² who found that pregnandiol continued to be excreted after the onset of menstruation, and oestrogen and androgen values were within normal limits.

The temperature investigations so far carried out show that length and amount of bleeding are in direct relation to the stage

of the luteal phase at which endometrial breakdown takes place. The later bleeding occurs in the luteal phase, the less it is in amount and duration.

Dysmenorrhoea.

The menstrual phase in cases of dysmenorrhoea is characterized by a premenstrual rise of temperature declining during or after cessation of bleeding, which may be interpreted as protracted progestin function (Figs. 14, 15 and 16). In cases in which both vaginal and oral temperatures were taken, in addition to the premenstrual rise the oral temperature rose to the same level as the vaginal curve. The oral tem-

perature being oestrogen-sensitive denotes, when it rises, a lack of oestrogen (Figs. 7 and 8).

It seems that in dysmenorrhoea the menstrual phase is characterized by protracted action of progestin in the absence of oestrogen activity.

This is in accordance with the experience of Hamblen¹³ that oestrogens relieve dysmenorrhoea, and with the opinion of Hirst and others¹⁴ that dysmenorrhoeic pain is of sympathetic nature and can be blocked out by antagonistic action of the parasympathetic. On the basis of Reynolds¹⁵ observations that oestrogens have a parasympatheticomimetic action mediated by

Fig.22

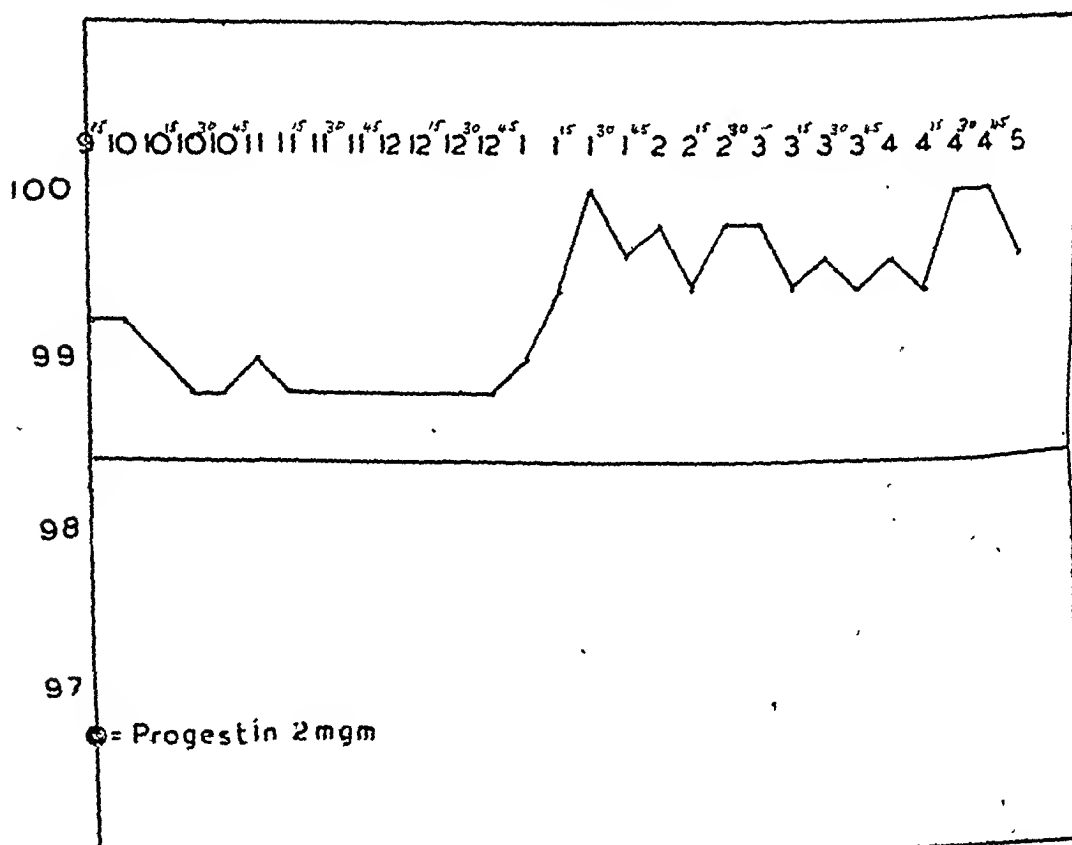


Fig.23

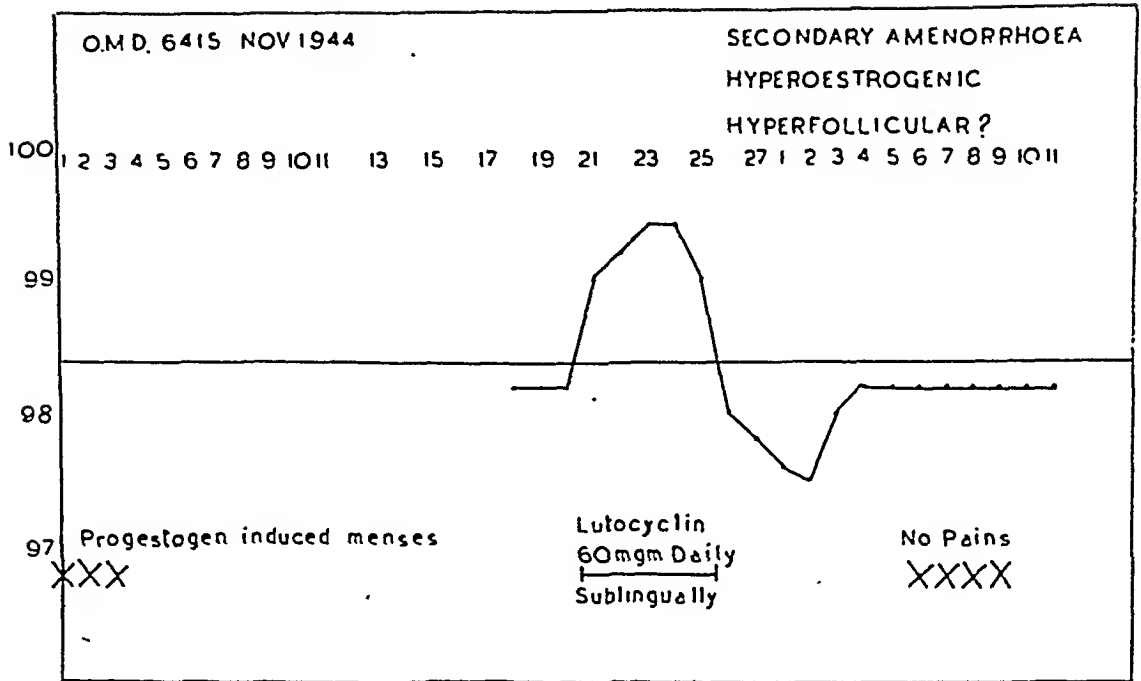


Fig.24

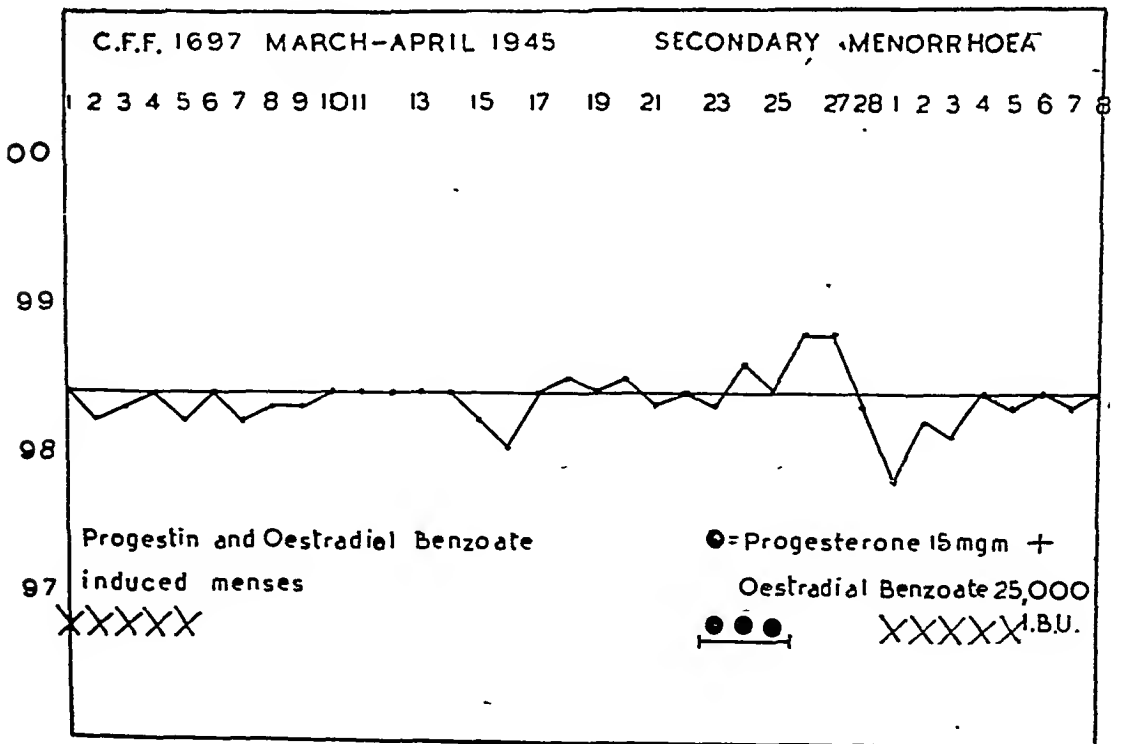
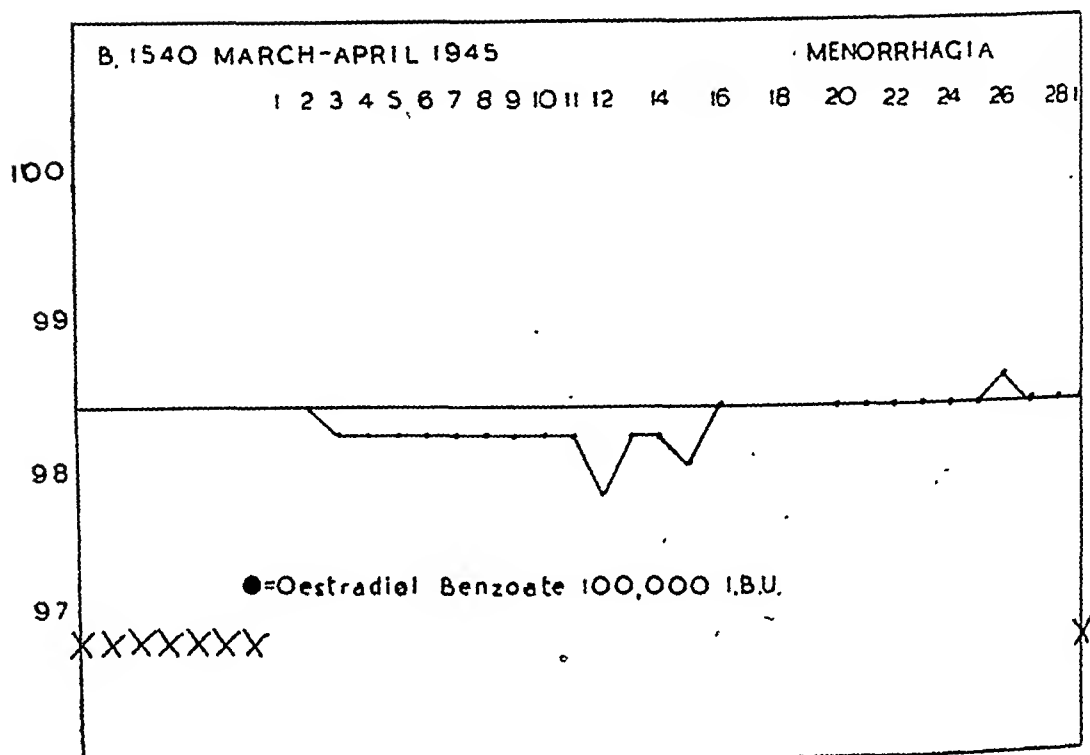


Fig.25



an inhibition of acetylcholine esterase, they conclude that dysmenorrhoea is a functional condition brought about by a relative deficiency of oestrogen which results in over-activity of the sympathetic nervous system, characterized by the production of vasoconstriction and pain. In the author's own experience administration of ethynil testosterone in the dosage of 300 mg. over 5 days to patients suffering from amenorrhoea frequently causes dysmenorrhoeic pain.

The mechanism by which protracted progestin activity combined with lack of oestrogen causes dysmenorrhoeic pain, is, on the whole, not quite clear. A better understanding is obtained if the precipitating factor of normal bleeding with the rôle of the ovarian hormones is closely examined. Oestrogen dilates the endometrial

blood vessels and increases their permeability,¹⁶ preventing undue congestion. Progestin causes a decrease in tonus of the uterine muscle enhancing congestion in the endometrium.

Little tissue loss occurs in hyperplastic bleeding whereas greater tissue loss takes place from a secretory type of endometrium.¹⁷ As functional dysmenorrhoea is almost always preceded by a secretory type of endometrium¹⁸ dysmenorrhoea is, mathematically expressed, equal to the process normally occurring in the secretory type of endometrium prior to bleeding, plus protracted corpus luteum activity, minus oestrogenic action.

In the normal cycle during the premenstrual phase, oestrogen and progestin withdrawal takes place, endometrial activity ceases, and rapid regression and shrinkage

of the mucosa occurs. This results in a disproportion between the length of the coiled arteries and the thickness of the endometrium. With further regression of the mucosa, more coils are formed retarding the blood flow and causing stasis.¹⁹ This precedes the flow by 1 to 3 days. Four to 24 hours before onset of bleeding, the coiled arteries become constricted at their base adjacent to the uterine musculature, and ischemic necrosis in the superficial parts of the endometrium results. Bleeding occurs by escape of blood from the capillaries and arterioles by diapedesis or through the degenerating walls.

In the dysmenorrhoeic endometrium only oestrogen withdrawal occurs while corpus luteum activity persists. This results in a delayed shrinkage and regression of

the mucosa and decreased tonus due to progestin activity, which produces increased engorgement not counteracted by the action of oestrogen. The resulting tissue loss and the unusual vascular engorgement seems to be the causative factor in dysmenorrhoeic pain.

Intermenstrual Bleeding.

Intermenstrual bleeding occurs with a very slight temperature rise of usually 0.2°F. only. This takes place within a monotonous curve on a high level and of only minor fluctuations (Fig. 17). It seems that the oestrogenic level is only slightly above the endometrial bleeding threshold. Therefore, only a small decrease in the oestrogenic level is necessary to precipitate bleeding. This is in keeping

Fig.26

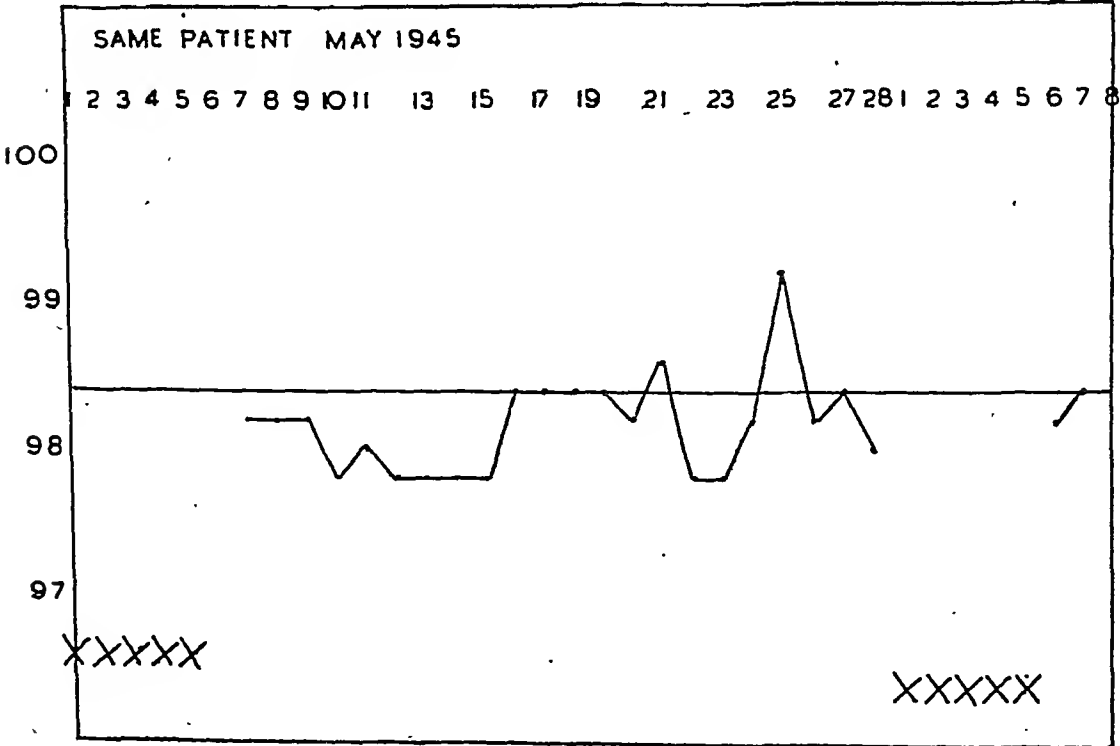
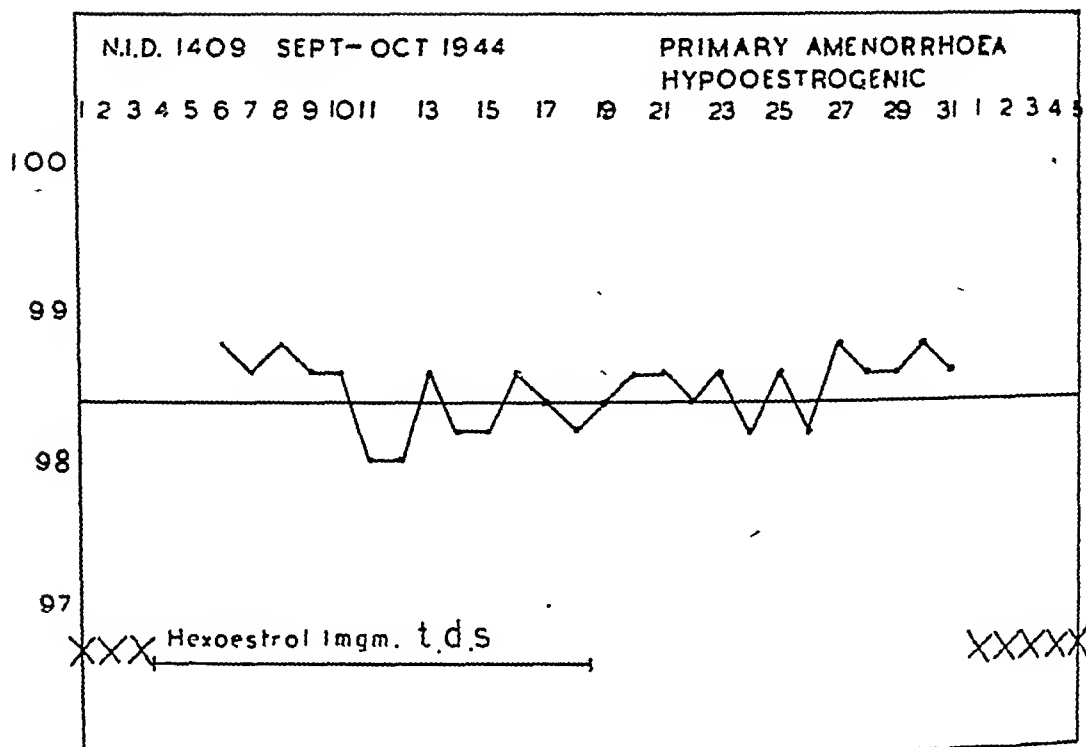


Fig.27



with Zuckerman's²⁰ observations that castrate monkeys receiving oestrogen in doses from 850 to 3000 I.U. daily did not bleed when the dose was reduced to 200 I.U. but a reduction to 150 I.U. was followed by bleeding of all monkeys within a few days.

Oestrogen, Progestogen, Androgen and Vitamin B Administration.

The observation of patients by temperature graphs has proved a valuable aid in diagnosing the effects of hormone treatment on the glands of reproduction. Furthermore, the study of temperature curves aids in deciding on the kind of hormone to be administered and its approximate dosage. A clear reflection of oestrogenic effects occurs in cases of amenorrhoea. It appears that oestrogen withdrawal bleeding is not as Novak²¹ stated: "to push the pendulum

of the rundown menstrual clock for a single idle incomplete beat when what we need is something to wind the clock" but causes, in many cases, stimulation to the pituitary gland (Figs. 10, 25, 28).²²

In fact, Eskin²³ demonstrated that injection of oestradiol benzoate into immature rats produced a release of gonadotrophic hormone from the anterior pituitary gland. The pituitary glands of the treated and controlled animals were examined, showing those of the treated animals to contain much less gonadotrophic substance than those of the untreated animals. The injections of oestradiol benzoate were followed by the formation of corpora lutea.

Oestrogen lowers temperature. However, graphs of patients under cyclic oestrogen treatment show frequently a sudden rise of temperature which starts during

oestrogen administration, maintaining a high level during the luteal phase, and is followed by menstruation (Figs. 20 and 28).

It is, furthermore, in keeping with the clinical evidence that amenorrhoeic patients who have undergone a 3 to 6 months course of oestrogen withdrawal bleeding, continue to bleed at regular intervals after cessation of treatment.

In one case the administration of ethynil testosterone 60 mg. daily for 5 days apparently stimulated increased release of F.S.H. from the anterior pituitary lobe (Fig. 23).

That progestin exerts a stimulating effect on the anterior pituitary has recently been demonstrated by Eskin²⁴ showing in the rabbit increased gonadotrophic activity following coitus after one injection of 0.5 Rabbit Units of progestin. Haemorrhagic follicles, rarely occurring after normal

coitus, were observed in rabbits treated with progestin prior to copulation.

There is a difference between the curve of morning and evening temperatures in reference to level, fluctuations and distance between the oral and vaginal curves. Particularly marked is the difference in those patients who are given treatment which elicits temperature changes (Fig. 4).

At the present stage of knowledge it is suggested that preferably evening temperatures are used for the investigation of cyclic changes in the woman. The taking of temperature in the morning is for many women inconvenient and frequently omitted in the early morning rush. In fact, most patients prefer to take their temperature in the evening.

The therapeutic effects are better reflected in the combined oral and vaginal

Fig.28

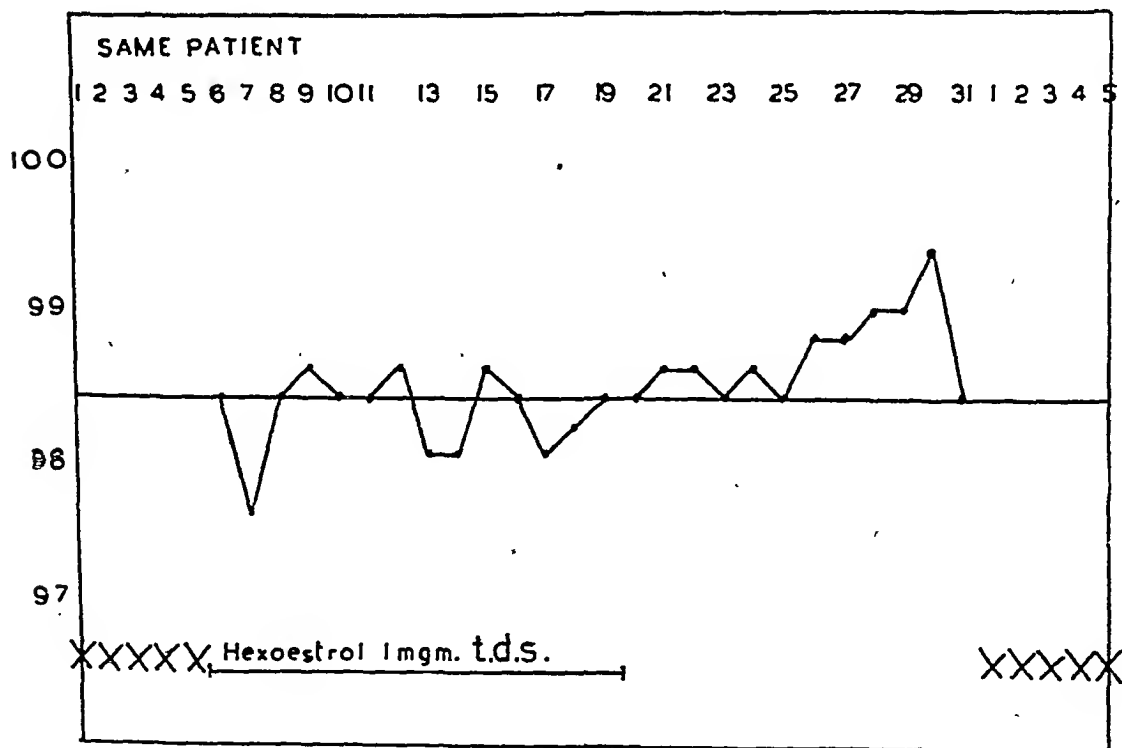
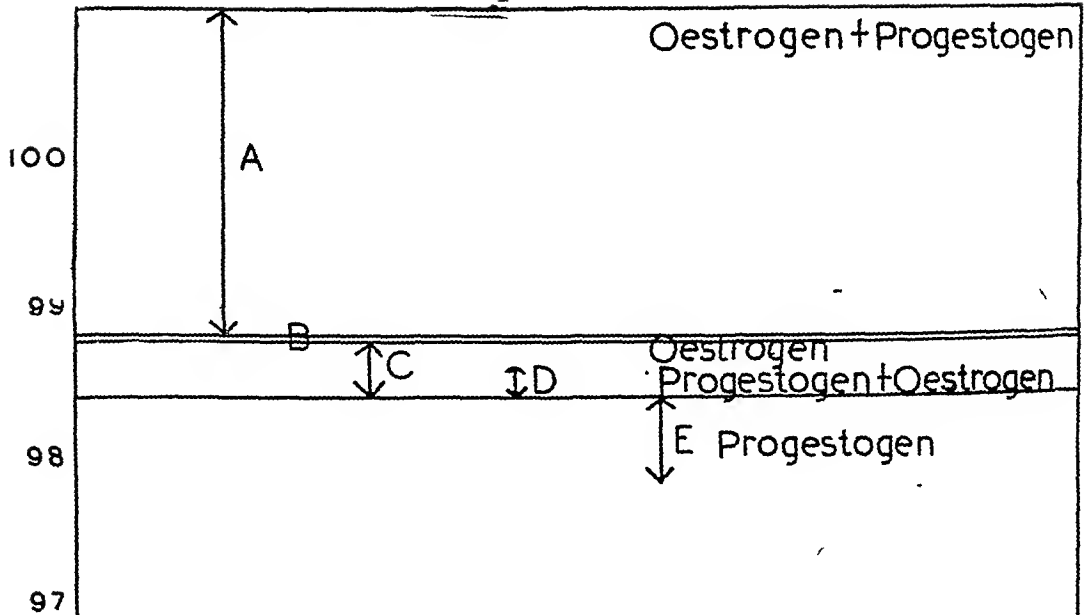


Fig.29



A = Severe oestrogen deficiency below bleeding threshold. Treatment = Cyclic oestrogen + progestogen

B = Bleeding threshold

C = Low oestrogenic level above bleeding threshold. Treatment = Cyclic oestrogen

D = Medium oestrogenic level.

Treatment = Progesterone 15mgm + oestradiol benzoate 25,000 I.B.U. intramuscular in 3 doses on successive days.

E = High oestrogenic level.

Treatment = Ethynil testosterone 60mgm sublingually daily for 5 days.

evening temperature graphs. However, for the investigation of general cyclic events in patients receiving treatment which may elicit temperature changes, the combined curves show a more regular pattern if recorded according to morning temperatures.

SUMMARY.

The vaginal and oral, or both temperatures taken simultaneously, were investigated in 41 women over 150 cycles.

The normal cycle shows a clear differentiation of its various phases, including ovulation.

In amenorrhoea, oligomenorrhoea, menorrhagia, dysmenorrhoea and intermenstrual bleeding, the temperature curves are of great diagnostic value. Special significance is attributed to the changing relation of oral and vaginal temperature in dysmenorrhoea.

In the therapy of menstrual disorders the temperature curve aids in deciding on the hormone and dosage to be administered, and indicates its degree of effectiveness.

The unmistakable sign of ovulation is of importance in cases of subfertility as well as for birth control owing to the easily recognizable safe and unsafe periods.

No objections have been encountered from patients who were asked to take their vaginal or oral temperature, or both simultaneously for many cycles.

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The Association of Erythroblastosis Foetalis and Accidental Antepartum Haemorrhage

BY

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ERYTHROBLASTOSIS foetalis, which develops most commonly when anti-Rh agglutinins is produced in an Rh negative woman by an antigen entering her circulation from her Rh positive foetus^{1, 2, 3, 4} has received much attention in the past 3 years.

Fifteen per cent of white persons are Rh negative and 12 per cent of marriages are between Rh negative women and Rh positive men, but the incidence of erythroblastosis is found by Potter, Davidsohn and Crunden⁵ at the Chicago Lying-in Hospital to be only 1 in 1,000 births. They thought that this disproportionately low incidence might be due to: (1) Childless or 1 child marriages; (2) variable potency of the Rh antigen of the infant in producing agglutinins in the maternal blood; (3) variable ability of the placenta to prevent the passage of the antigen; (4) variable maternal response to the introduction of the Rh antigen into the bloodstream; (5) variable ability of the placenta to prevent the passage of the agglutinins.

As regards the first point, Hogben⁶ states "that it is certain in the light of statistics already to hand that second or later born heterozygous offspring of Rh negative mothers by Rh positive fathers are far more numerous than recognizable cases of neonatal haemolytic anaemia and associated miscarriages or stillbirths."

Boorman, Dodd and Mollison⁷ noted the failure of correspondence between titre of agglutinins and severity of the disease,

so that variable potency in the Rh antigen in the infant (unless the antigen has been introduced by previous transfusion of the mother with Rh positive blood), variable maternal response, and variable permeability of the placenta for antigen and agglutinins are the important factors.

The mode of passage of the Rh antigen, thought to be confined to the red cells, across the placenta has puzzled everyone, and Lubinski, Benjamin and Streat⁸ considered it impossible unless some pathological conditions were present. Javert⁹ found haematomas in the intervillous spaces in 8 out of 35 placentae from cases of haemolytic anaemia of the newborn.

In 2 out of 3 cases of erythroblastosis occurring in 6 months (April to September 1944) at Queen Charlotte's Hospital, there was premature separation of the normally implanted placenta with antepartum haemorrhage. As both these mothers had previously borne only healthy children, it seemed possible that the haemorrhage from the placental site with rupture of the maternal sinuses and consequent damage to the placenta might be the factor allowing transmission of antigen and agglutinins. As both conditions (i.e. premature separation of placenta and erythroblastosis) are comparatively rare, although the number of cases was small, these facts suggested that the association might be of some significance.

A careful study of the literature revealed

little. Schwartz and Levine⁹ had found some association between the two conditions. In 1937 a woman transfused for intra- and postpartum haemorrhage at the delivery of a macerated foetus, had a severe reaction after transfusion with her husband's blood. She was found to be Rh negative and her husband Rh positive. They also found that in 4 cases of stillbirth associated with premature separation of the normally implanted placenta, 2 were due to erythroblastosis, but concluded that the foetal death almost certainly antedated the premature placental separation, and suggested that "although most cases of premature separation of the normally implanted placenta do not appear to be accompanied by erythroblastosis," analysis of a longer series was indicated.

Accordingly, with the help of Dr. Allott of Lewisham Group Laboratory, all cases of antepartum haemorrhage occurring at St. Alfege's Hospital, between February and June 1945, were investigated with the following results:

1. Placenta praevia: 6 cases.

Rh reports are available in only 5 of these, and all were positive.

(Genotypes in 4 where they were determined, were Rh₂rh, Rh₁Rh₂, Rh₂rh, Rh'rh.)

2. Accidental antepartum haemorrhage, mother Rh negative, father Rh positive; * 5 cases.

3. Accidental antepartum haemorrhage, mother Rh positive; 5 cases.

4. Antepartum haemorrhage, placental insertion not determined, mother Rh positive: 1 case.

5. Accidental antepartum haemorrhage, mother and father both Rh negative: 1 case.

The tables give details of the pregnan-

cies in groups 2 to 5, and of the 2 cases from Queen Charlotte's Hospital (*vide supra*.)

The series is small and the full scope of the blood investigations necessary is only now being realized, as with Cases 3a and b, so that a great deal more work is necessary. Later Dr. Allott and I hope to publish a report on this work.

In the meantime, the following facts emerge from the St. Alfege's series of cases. Five out of 10 (50 per cent) of the mothers who had an accidental antepartum haemorrhage were Rh negative with Rh positive husbands* and 3 of these had anti-Rh agglutinins. Of the 3 who were delivered soon after the antepartum haemorrhage, 1 had a child with only a moderate degree of jaundice, who recovered without transfusion, another a child with very gross hydrops, and the 3rd a child stillborn, possibly as a result of the course of labour. In the 2 mothers who were not delivered until some weeks after the first haemorrhage, the foetus was stillborn, macerated, and of a size corresponding roughly with death at the time of onset of the bleeding. Of the cases with Rh positive mothers, in only 2 were Rh genotypes determined; the mothers were found to be Rh₂rh and Rh₁rh, with children Rh₁Rh₂ in each case. This could theoretically make possible the development of the less common Γ and H antibodies in the 2 mothers, but evidence of their presence was not found.

It is too early to dogmatize, but it would seem justifiable to conclude that the woman in whom iso-immunization can occur, is abnormally prone to accidental antepartum haemorrhage, and the ensuing placental damage may be a factor in transmission of antigen and agglutinin. There seems, except in case 2d, to be an association between the time between delivery and bleeding and the severity of the erythroblastosis and titre of the agglutinins.

* Except the husband of Case 2g, who cannot be tested.

TABLE OF CASES.

| Mother's blood | | anti Rh agglutinins | Father | Other children | Fate of pregnancy | Notes on pregnancy and labour |
|--|-------------------------|--|---|---|--|--|
| (2) <i>Accidental Antepartum Haemorrhage in Rh negative Mothers. (Queen Charlotte's Hospital).</i> | | | | | | |
| 2a. | Group A. Rh negative | Doubtful | Rh + ve | (1) Died age 3½ months (2) 3 months miscarriage (3) Alive and well (4) Alive and well (Toxaemia of pregnancy) 1939 | Live male infant, 3½ pounds. Developed jaundice, spleno- megaly and hepatomegaly. Recovered. Group O Rh + ve. | Risk haemorrhage at 12/12. Artificial rupture of membranes; placenta not felt. Spontaneous delivery 10 hours after first haemorrhage. |
| 2b. | Rh negative | Unknown | Unknown | (1) Alive and well | Live female infant, 2½ pounds. Developed jaundice and haemolytic anaemia. Recovered. Rh + ve. | Slight to moderate continuous loss from 17 hours before onset of labour until delivery at 20½ Placenta not felt. Spontaneous delivery 2½ hours after first haemorrhage. |
| (2) <i>Accidental Antepartum Haemorrhage in Rh negative Mothers. (Saint Allege's Hospital).</i> | | | | | | |
| 2c. | Group O. Rh negative | 10 days antepartum incomplete antibody in 1/64 dilution: 7 days in 1/128 dil: | Group B. Rh ₁ Rh ₁ | (1) Twins (a) stillborn (b) alive and well Rh ₁ rh (2) Stillborn (3) Stillborn | Macerated foetus about 26/52 | Irregular scanty haemorrhage from about 21/52. Movements not felt from 29/52. Further haemorrhages in hospital 1 and 6 days before delivery. Repeated medical inductions resulted in spontaneous delivery 16½ after last period. |
| 2d. | Group A. Rh negative | Very doubtful | Rh + ve | (1) Alive and well Rh + ve 1910 (2) Alive and well Rh + ve 1912 (3) Stillborn | Macerated foetus about 26/52 | Four moderately severe haemor- rhages from 39/52, movements ceasing after the first. Fetal heart not heard on admission. Repeated medical inductions given. Delivery complicated by further haemorrhage and severe postpartum haemorrhage requir- ing transfusion. |
| 2e. | Group A. Rh negative | None detected | Rh + ve | (1) Alive and well (Not available for testing) | Live male infant 1½ pounds. Slight jaundice in early days; slow in gaining weight. Rh + ve. | Moderately severe antepartum haemorrhage at 31/52 followed by onset of labour. Artificial rup- ture of membranes; as over but dilated; placental edge just felt in lower segment. Spontaneous delivery 22 hours after first haemorrhage. |
| 2f. | Group O. Rh negative | 1st day p-p doubtful, 4th day p-p in 1/64 dil: 20th day p-p in 1/256 dil: | Rh ₁ Rh ₂ | (1) Alive and well (2) Alive and well Rh ₁ rh (3) Stillborn—premature (4) Alive and well Rh ₂ rh | Very gross hydrops foetalis. Lived a few minutes only. | Admitted as hydramnion. X-ray suggested hydrops. During the night developed severe antepar- tum haemorrhage. Caesarian section performed. Placenta in- serted in upper segment. |
| 2g. | Group O. rh Yh | None 2 months after delivery | Not available | (1) Alive and well | Stillborn. P.M. showed asphyxia. | First seen at term with antepar- tum haemorrhage, not in labour. Artificial rupture of membranes. Placenta not felt. Very strong pains. Deposition of prothrombin on both arms was necessary. |

TABLE OF CASES.

| Mother's blood | anti Rh agglutinins | Father | Other children | Fate of pregnancy | Notes on pregnancy and labour |
|---|---------------------|--------------|-------------------------------|---|--|
| (3) <i>Accidental Antepartum Haemorrhage in Rh positive Mothers. (Saint Allege's Hospital).</i> | | | | | |
| 3a. Group O. Rh, rh | | Unobtainable | (Primigravida) | Live female infant, 4½ pounds Slow in gaining weight Group O, Rh, Rh, | 34/52 admitted with very severe antepartum haemorrhage. Caesarian section performed—much haemorrhage into uterine muscle. Placenta in upper uterine segment. |
| 3b. Group B. Rh, rh | | Unobtainable | (1) Alive and well | 1942 Live female infant, 6 pounds Group O, Rh, Rh, | Slight loss just before onset of labour, increasing after rupture of membranes and becoming profuse as head appeared at vulva. Forewaters delivered. Point of rupture of membranes 4 inches from placental edge. |
| 3c. Group O. Rh + ve | None | Unobtainable | (1) Alive and well | 1941 Live infant, 8½ pounds. | Small bright red loss before admission at 30/52. Discharged herself against advice. Spontaneous delivery at 40/52 |
| 3d. Group O. Rh + ve | None | Unobtainable | (1) Alive and well | 1937 Live infant, 7½ pounds. | Bright red loss at 32/52. Examined at 36/52. Placenta not felt. Spontaneous delivery at 38/52. |
| 3e. Group A. Rh + ve | None | Unobtainable | (Primigravida) | Live male infant, 8 pounds. | Very slight haemorrhage at 34/52. Blood pressure 150/110; slight albuminuria. Toxaemia resolved very rapidly. Examined at 36/52. Placenta not felt. Normal delivery at 40/52. |
| (4) <i>Antepartum Haemorrhage—Placental Insertion not Determined. (Saint Allege's Hospital).</i> | | | | | |
| 4. Group O. Rh + ve | None | | (1) Alive and well Rh + ve | 1941 Live infant, 5½ pounds. Group O, Rh + ve. | Repeated small haemorrhages from 29/52. Spontaneous delivery at 34/52. Placental insertion not determined by vaginal examination |
| (5) <i>Accidental Antepartum Haemorrhage—Mother and Father both Rh Negative. (Saint Allege's Hospital).</i> | | | | | |
| 5. Group O. rh rh | | rh rh | (Primigravida) | Infant lived only a few minutes. Cord blood unobtainable. | Scanty irregular haemorrhage from 28/52. Rupture of membranes at 36/52 for severe toxemia. Placenta not felt |

Whether in such cases the risk to the baby from erythroblastosis is greater than the risk from prematurity; and that therefore induction rather than expectancy should be the line of treatment when possible, it is as yet impossible to say.

One fact is certain, the woman with antepartum haemorrhage is often likely to need a blood transfusion. Except in those units fortunate enough to be able to have all expectant mothers Rh-tested, or have a blood bank of only Rh negative blood, there is a grave risk of incompatible transfusion being given.

I have to thank Dr. Allott for his enthusiasm and untiring co-operation without which I could not have proceeded. My thanks are also due to the medical staff of Queen Charlotte's Hospital and to Dr. Young, Medical Superintendent and Miss Fleming, Obstetric Consultant, St. Alfege's Hospital, for permission to publish these cases.

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A Morphological Study on Chorioepithelial Proliferations (Based on 10 cases).

BY

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THE basic principles of pathology are known to all but in the morphological study of human trophoblast—normal or pathological—difficulties arise in the proper interpretation of the findings. These are due to the complicated process of amalgamation of ovum with mother and the peculiar behaviour of the elements involved. So it is necessary to recapitulate the physiological changes in the early stages of normal placentation in order to appreciate the pathology of chorionic epithelium.

From a study of descriptions of placentation by Grosser,¹ Streeter,² Brewer and Fitzgerald,³ Rock and Hertig,⁴ and many others, explanation experiments *in vitro* by Friedheim,⁵ Maximow,⁶ and Sengupta,⁷ as well as personal observations, an attempt will be made in this paper to elucidate more fully the relation of early trophoblastic development to either the normal or penetrating placenta, the simple or destructive hydatidiform mole, or, finally, the malignant variety of chorioepithelium—the chorioepithelioma.

PHYSIOLOGY OF THE TROPHOBLAST.

The modern conception of the trophoblast is that it produces the chorionic epithelium with all its cell types. Thus the polygonal cells or cells of Langhans and the syncytial cells must be considered to be successive stages of differentiation. In the

earliest stages of development the trophoblast consists only of Langhans' cells which are able to propagate by cell division and to infiltrate and to destroy tissues like a malignant tumour. On the other hand the syncytium must be regarded as a secondary formation. This does not mean that it is purely a degenerative product. On the contrary, its cells display marked biological activity in their proteolytic ability to nourish the foetus in its early stages of development by liquefying the maternal tissues at a time when foetal villous vessels are not yet formed. The formation of syncytium apparently takes place whenever Langhans' cells come in contact with liquid material, or local conditions become less suitable for cell nutrition. This explains the appearance of syncytium in non-liquefied tissues. There are other kinds of chorionic cells which are important, especially when considering the pathology of the trophoblast. These have been described by different authors as "syncytial giant cells" or "migrating" or "chorionic single cells." Their origin from the cellular columns of the trophoblast has been definitely accepted as the result of Meyer's studies on this subject. They may appear far from the placental site and can maintain themselves in the maternal tissues for a long period. Finally, mention must be made of the fibrinoid coagulation, product of degeneration of chorionic epithelium and maternal tissues. Grosser¹ first drew

attention to its homogeneous and more clumpy shape in contrast with the more fibrillar shape of blood fibrin. According to Meyer,⁹ this fibrinoid coagulation must be considered a phenomenon of regression which is due to the struggle between foetal and maternal tissues and appears also as a demarcation zone between less vital tissues. Thus this fibrinoid coagulation is to be found always at contiguous surfaces in the so-called "stripe of Nitabuch." It can also be seen at the sites of irregular proliferation of the chorionic epithelium either in marginal vessels or in the depths of the myometrium. The stripe of Nitabuch may be considered as a kind of barrier against the invading trophoblast. It varies in thickness with the result that where it is particularly dense it will entirely check the progress of the invading trophoblast.

As soon as the trophoblast has developed its power to dissolve the maternal tissues the ovum imbeds itself wherever it may be situated at the time. At first these tissues become entirely liquefied but gradually the defence of the maternal body grows stronger, whereas the power of the blastic invasion weakens. Thus, the chorionic epithelium becomes intermingled with the maternal tissues and the ovum settles down within the maternal substance only by the action of the chorionic epithelium. All this occurs in the so-called "penetration zone" (Grosser) and this stage of trophoblastic development is described by Meyer⁹ as the "histiotrophic" phase, which means that the trophoblast nourishes itself at the cost exclusively of the maternal tissues. This phase is marked by many changes leading gradually to the "haemotrophic" phase and the formation of the true placenta. The trophoblast has generally fulfilled its task within the first 8 or 10 weeks of pregnancy and later disappears, leaving behind only the epithelium of the villi. It is important

to bear in mind that during the histiotrophic phase a foetal stroma does not exist generally, but where it does form, for example, in the first generation of villi, it has no biological function since it is not vascularized. Meyer⁹ stresses this fact and calls this type of growth "cytotypic" as distinct from the "histiotypic" form of growth during the haemotrophic phase just mentioned. An appreciation of these different types of growth is essential, since it is only the first type, namely the "cytotypic," that is found in the chorionepithelioma, which thus occupies a unique position in human pathology.

It has been necessary to consider in full the features of the trophoblast's normal development since a knowledge of these is essential when one has to give an opinion on chorionic invasion, on abnormally active proliferation of chorionic epithelium, or whether a growth is benign or malignant. The basic elements which compose the final picture of all such cases are identical. They consist of:

- (1) An unlimited power of destruction in the cells of the young trophoblast.
- (2) The maternal defence-mechanism which comes into full action only slowly and progressively.

The occult potentialities and mutual balance of these factors are sometimes impossible to assess even by one who has had much experience in pathology.

Some of these difficulties in diagnosis regarding chorio-epithelial proliferations will now be described.

A. CHORIONIC INVASION.

Meyer⁸ first emphasized the importance of the chorionic giant cells and their origin from the chorionic epithelium. In the literature of the distant past these cells have often been mentioned in connexion with so-called atypical cases of chorionepithe-

lioma. Meyer, and before him von Franqué,¹⁰ doubted whether single chorionic cells were characteristic of a malignant tumour unless they appear in accumulations of cells—the third irregular type of chorionepithelioma (Marchand). Franqué was always surprised by the astonishingly high rate of complete recovery in cases of irregular chorionepithelioma with isolated cellular proliferation. Meyer⁸ has clarified this problem by demonstrating that single chorionic cells in varying numbers were often to be found at the site of placentation, proliferating from the cell columns of the trophoblast into the decidua and even muscle layers. At the 4th or 5th month of pregnancy these cells are to be found in their greatest number and by the end of pregnancy they have become much fewer. On the other hand they may be observed in much larger numbers in the case of pregnancy in an abnormal uterus, where there is hypoplasia or atrophy of the mucosa, in endometriosis, or in an abnormal pregnancy such as hydatidiform mole or placenta praevia. Thus one can say a fully developed decidua acts as a sort of barrier against the abnormal proliferation of chorionic elements. Even if these cells are found in excessively large numbers, provided placental remains are present at the same time, there is no need for alarm. By the 4th week after delivery or abortion they have usually disappeared. But if these cells are found in rather considerable numbers after this time, without any other morphological changes due to pregnancy, then one must view the case with suspicion. In such a patient the pathologist should advise that a clinical examination and a quantitative estimation of the gonadotropic hormone in the urine be carried out every 2 or 3 weeks. If the findings are at first negative and later the test becomes positive, or if there is an increasing amount of gonadotropic hormone in

the urine, then there is no doubt as to the existence of a chorionepithelioma or a destructive hydatidiform mole (Clausberg,¹¹ Ehrhardt and Bureck¹²). Four cases will now be described illustrating chorionic invasion. The cases were diagnosed as abortion 2, myoma 1, rupture of the uterus 1.

CASE 1. 837/40.

Patient aged 25. Amenorrhoea for 3 months. One week before admission to hospital had acute abdominal pain and some uterine bleeding. Diagnosis, abortion. Treatment, curettage.

Histology of curettings: blood, uterine muscular fibres and irregularly formed endometrium. Mucosa generally rich in glands of a multiform type. No active secretion. Stroma variable in its structure; sporadic formation of decidua compacta and small areas of dense inflammatory infiltration. In some places there are large irregularly-shaped strips of fibrin. Around the vessels there are big decidual cells mingled with much fibrin. In some parts the decidua reaches deeply into the muscular layer where large cells are rather frequently seen between the muscular fibres. Even with low power these cells, by reason of their irregular shape and darker colour, can be easily differentiated. They are found particularly near the vessels. They have one or several large round or ovoid nuclei and can be easily distinguished from the large decidual cells.

Diagnosis: Endometrium in a state of puerperal regression with inflammatory infiltration. Excessive proliferation of chorionic cells in the muscular layers of the uterus (chorionic invasion). No sign of malignancy in the material examined.

CASE 2. K.I. 3/39.

Patient aged 30; 5 years ago normal delivery; 2 abortions, 1 before and one after the delivery. No amenorrhoea but 2 short uterine haemorrhages a fortnight after the last normal period. Curettage. A small soft area was found on the posterior wall of the cervical canal.

Histology of the curettings: (Professor Oberndorfer, late Director of the Cancer Research Institute, Istanbul University.)

Puerperal stroma, vessels in regression, compressed gestational glands. Stroma extensively infiltrated by giant cells containing a few or many nuclei, as well as smaller giant cells resembling common decidual cells. Inflammatory infiltration (Fig. 1).

Diagnosis: ? Hyperplasia of decidua. ? Chorionic invasion. No sign of malignancy in the material examined, but further observation of the patient is recommended.

CASE 3. G. 3/38.

Clinical data not available. Operation specimen of a uterus removed by subtotal hysterectomy.

Macroscopic findings: Myoma, size of a small apple, and, in addition, a round red area the size of a hazelnut, within the uterine muscle in the neighbourhood of one tube.

Histological findings: Muscle very vascular and containing detached endometrial glands. At one side of the section there is an area of compact round-cell-infiltration with some hyalin connective tissue. The patch of red necrosis observed macroscopically is adjacent to this area. The necrotic region consists of fibrin and blood and is everywhere surrounded by swollen fibrinoid coagulated muscle-fibres and strips of hyaline connective tissue. Big irregular cell-elements with large, compact and darkly stained or vacuolized nuclei are observed here very frequently. Within this region no signs of inflammatory infiltration (Fig. 2).

Diagnosis: Myoma of the uterus. Slight adenomyosis interna. Giant-cell-proliferation around a necrotic area (chorionic invasion).

CASE 4. 817/38.

Patient aged 22; 3-para, 7th month of pregnancy.

Clinical diagnosis: Internal haemorrhage (? rupture of the uterus).

Treatment: Vaginal hysterectomy.

Macroscopic findings: A hole, diameter 2 cm., at the fundus uteri. Edges round and thick; at other places the uterine wall is particularly thin. Placental remains not seen.

Microscopic findings: Typical puerperal changes. At the placental site there is a more or less clearly visible stripe of Nitabuch separating the maternal from the foetal elements. Here there are large cellular accumulations, rather similar to the cell-

columns of young trophoblast. At some other parts of the placental site separation of the maternal and foetal tissues is not so marked. At such places one finds an extensive invasion of large, irregularly shaped, one- or multi-nucleated cells, which can be seen deep in the muscular layer also. These cells form short lines and are surrounded by some inflammatory cells. The muscle-fibres next to the serous coat of the uterus are in some places replaced by connective tissue poor in nuclei.

Diagnosis: Spontaneous rupture of the uterus. Persistence of the trophoblast. Chorionic invasion.

DISCUSSION.

In Case 1 there can be no doubt that the changes are benign. The histological picture is that seen after an ordinary abortion. Even though there is considerable chorionic infiltration it is not of much importance. However in Case 2 the cellular invasion is so striking that it seems easy to diagnose the condition as malignant. Professor Oberndorfer leaves the question open as to whether the case is one of excessive decidual reaction or chorionic invasion. I incline to the latter interpretation. Firstly, in cases with hypertension of decidua, giant-cell-formation is generally not so marked as in this case. Secondly, large parts of the stroma do not show decidual reaction at all, and infiltration is most widespread in regions where there are digitations of muscle-fibres into the mucosa. Thirdly, there is the clinical evidence of the soft area in the posterior wall of the cervical canal suggesting an unusually low nidation of the ovum. This would also support my view that this is a case of simple chorionic invasion. Case 3 is incomplete through lack of clinical data. The pathologist can describe only the presence of chorionic invasion following a supposed recent pregnancy. This diagnosis might be disputed on the insufficiency of clinical detail. However, one can exclude a giant-cell-reaction around a foreign body as well as

a regenerative reaction of muscle with formation of myogenic giant cells from the general histological picture. That the presence of a myoma and an endometriosis in this specimen would stimulate chorionic invasion is shown by de Snoo and Stroink.¹³ In Case 4 the main findings are old scarring in the uterine wall, chorionic-cell-invasion and a partial persistence of the trophoblast. An exact evaluation of the aetiological relation of these facts is difficult. One is inclined to assume that the lesion of the uterine muscle may probably have induced the foetal parts to more intensive growth, which is further suggested by the presence of cell-columns in a rather late stage of pregnancy. There is, on the other hand, no morphological proof that the clinical catastrophe was mainly due to this fact. For the explanation of the rupture the presence of scars in the uterine wall seems quite sufficient. But, so far as the problems dealt with in this paper are concerned, it is interesting that the histological findings point to the existence of that intimate reciprocal interference of maternal with foetal parts mentioned in the introduction.

B. CHORIONIC PROLIFERATION TOGETHER WITH VILLOUS STROMA.

Examples will now be given of increased proliferative power of the chorionic epithelium. One case is a spontaneous rupture of the uterus, and the other two are hydatidiform moles.

CASE 5. 847/39.

Patient, aged 25, admitted to hospital moribund. Uterus, size of a 7 months' pregnancy.

Diagnosis: Internal haemorrhage.

Autopsy: Three litres of fresh blood in the abdominal cavity. On the fundus of the uterus, which contained a normal pregnancy of 5 months, there was a bluish, round area 0.5 cm. in diameter through which chorionic villi were protruding.

Examination after fixation revealed extreme general thinning of the uterine wall, a small rupture at the fundus and imminent rupture at 2 other places, where the uterine wall was about 1 mm. thick.

Microscopic findings: Destruction of uterine wall at the site of the rupture. Muscle shows extensive fibrinoid degeneration in some parts, and in others complete necrosis. Villi appear to be boring into the uterine wall, and chorionic elements, singly or in masses, are eroding and even completely obstructing the vessels (Figs. 3 and 4).

Diagnosis: Spontaneous rupture of the uterus "placenta percreta."

CASE 6. 193/40.

Patient, aged 18, moribund. Uterus 6 months in size; excessive bleeding *per vaginam*.

Autopsy: Uterus 22 by 14 by 10 cm. with cystic ovaries. Peritoneal surface regular. Cavity contained hydatidiform mole of medium size, grape-like clusters with much blood and clot. Uterine wall of regular thickness of about 1 cm. Only at the placental site was the wall somewhat thinner. Vessels engorged with blood. Apart from the presence of a mole and absence of a foetus the uterine topography was that of a normal pregnancy. Decidua vera with an average thickness of 2 mm. was clearly seen and lifted from the underlying tissues. The serotina is generally well formed but variable in thickness. Fallopian tubes twisted, abdominal ostium open. Each ovary about the size of a hen's egg and consisting of several small cysts with a yellow surround.

Microscopic findings: Uterine wall at site of molar attachment (from within out, Fig. 5), molar tissue consisting of large villi with rather dense or dropsical stroma and double layered epithelium; decidua compacta contains much fibrin; decidua spongiosa in this situation does not show important pathological changes, but clear demarcation from the muscular layer which has enlarged veins filled with erythrocytes and inflammatory cells. But in other places the spongiosa and layer of fibrin are greatly reduced in their thickness and there is no line of distinction between them. In general the chorionic elements have not passed through the fibrin into the deeper layer of the decidua, but there are places where they reach the muscular layer in large numbers followed closely by villi. In nearby areas both layers of the mucosa

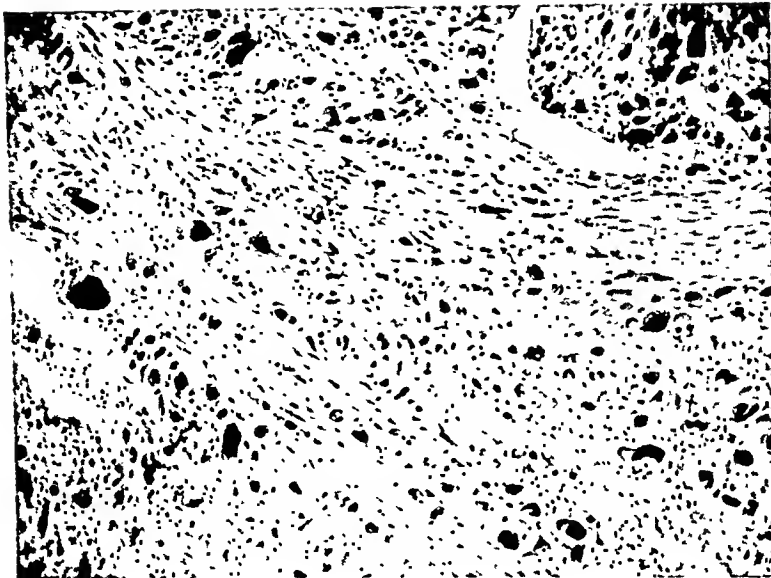


FIG. 1 (CASE 2).

Endometrium showing infiltration by many mono- and multinuclear giant cells.

x 60



FIG. 2 (CASE 3).

Uterine wall showing giant cell infiltration around necrotic area.

x 21.

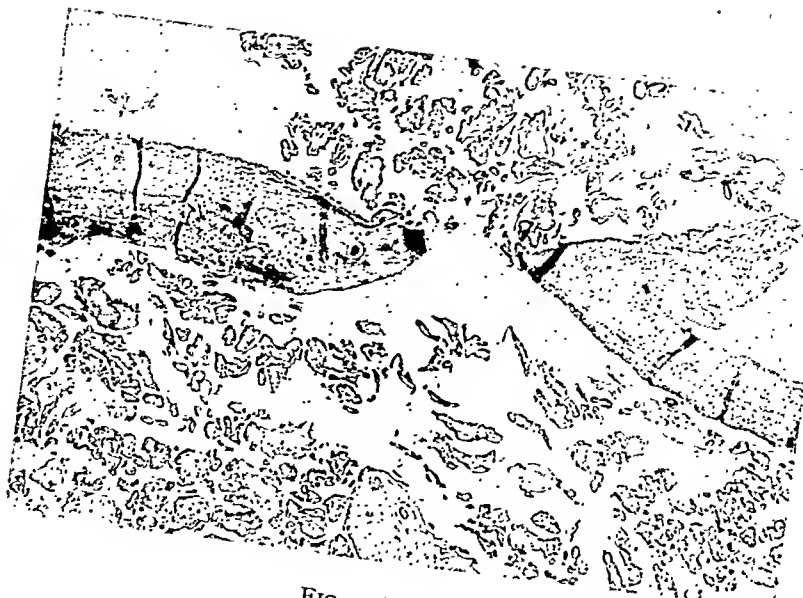


FIG. 3 (CASE 5).
Uterine wall at site of rupture.
x 6.



FIG. 4 (CASE 5).
Uterine wall showing at (1) attachment of chorionic villus directly to muscle,
at (2) enlarged vessels containing many chorionic cells.
W.A.L.

x 21

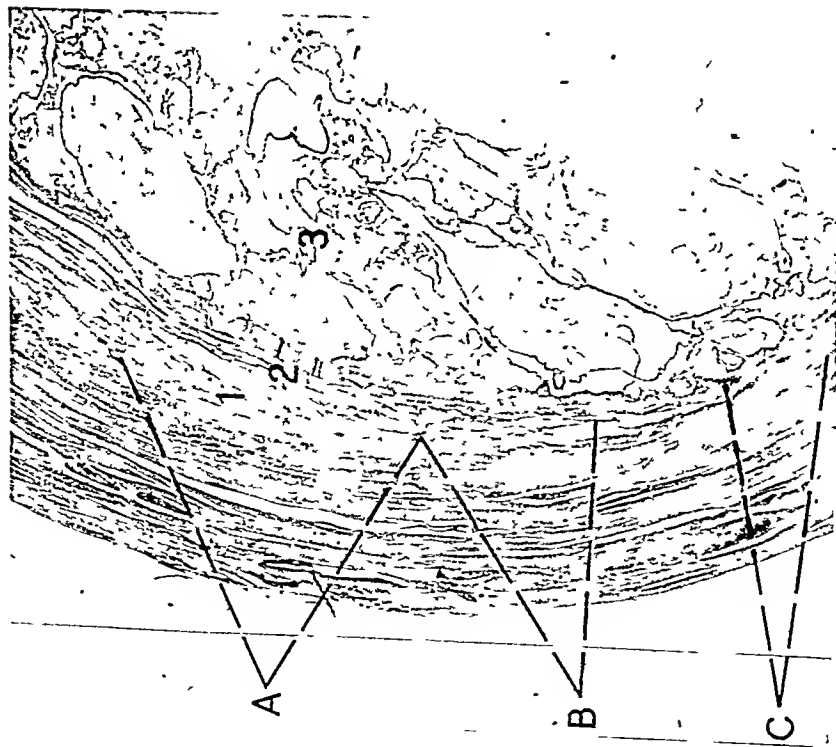


FIG 5 (CASE 6).

- Hydatidiform mole *in situ*. Placental site.
- A. Shows region of fully-developed mucosa (1) and wide fibrin layer (2) between mole (3) and mucosa.
- B. Shows thinning of mucosa.
- C. Shows direct contact of mole with muscle.
- W.A.L. x6

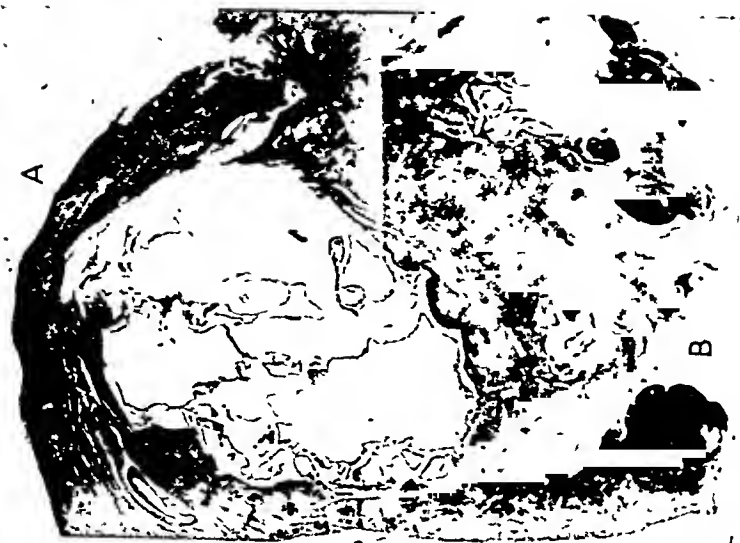


FIG. 6 (CASE 7)

Composite photomicrograph of transverse section of uterine wall.

- A Peritoneal surface. B Cavity.
- Typical of destruct ve hydatidiform mole. x4

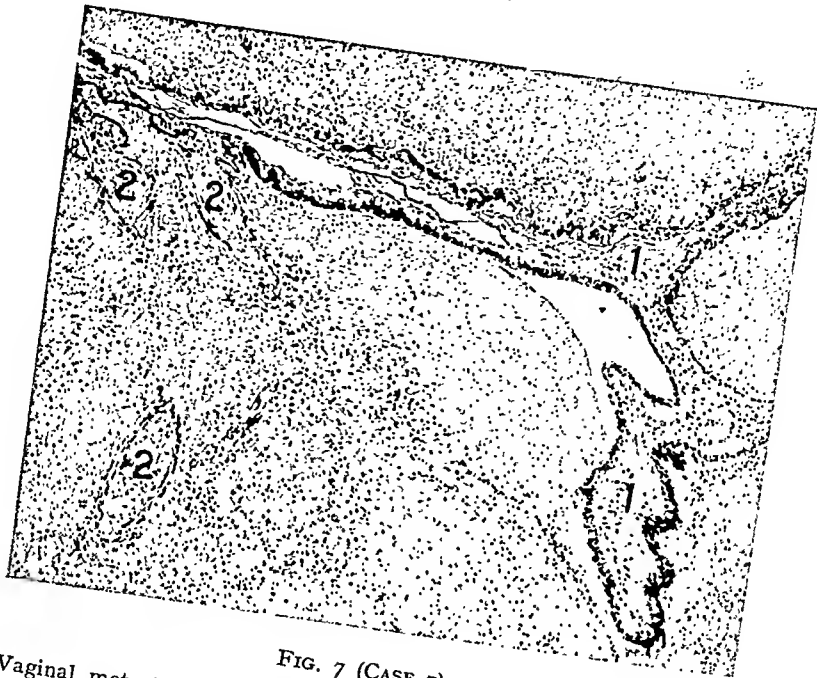


FIG. 7 (CASE 7).
 Vaginal metastasis showing large well-formed placental villus (1)
 and placental villi without epithelium (2).
 x 21

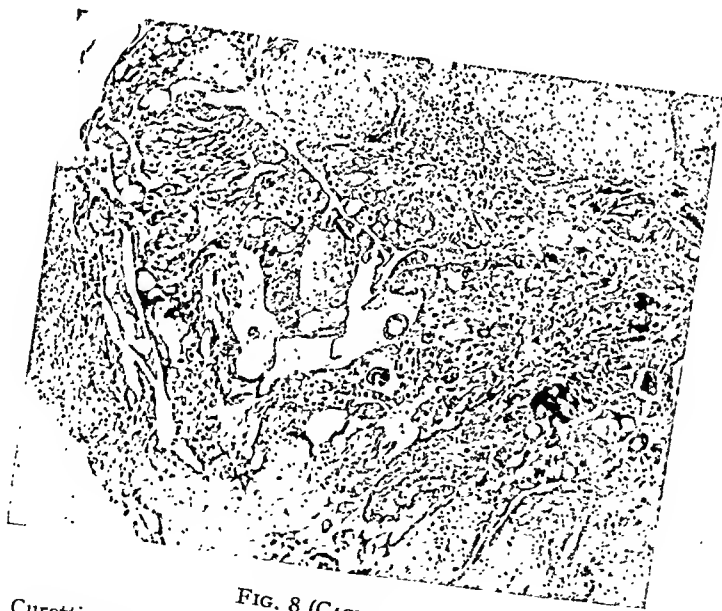


FIG. 8 (CASE 10).
 Curetting showing the only area where chorionic elements
 were present and on which the wrong diagnosis of chorion-
 epithelioma was based.
 W.A.L.
 x 21

seem to have disappeared owing to the massive infiltration of chorionic cells disregarding any pre-existent layers and undermining the margin of the neighbouring tissues. Here even the superficial venous sinuses are open and are invaded by chorionic cells which, however, are still attached to villi. The penetrating elements consist mainly of small Langhans' cells with very few syncytial cells. Few degenerative changes are to be seen in these cells and haemorrhagic areas are rare.

Uterine wall opposite to molar attachment: Normal decidua compacta with a wide spongiosa is sharply delimited from the muscle layer. Vessels open and enlarged.

Specimens from the centre of the mole: These show different degrees of epithelial proliferation. Syncytial elements observed more frequently. The average extent of the epithelial proliferation is not excessive.

Diagnosis: Hydatidiform mole *in situ*.

CASE 7. 506/41.

Patient, aged 22. Admitted to the hospital in a very anaemic state. Examination revealed hydatidiform mole, which was removed *per vaginam*. Two months later the patient returned because of uterine bleeding and a small nodule at the introitus. While in hospital there was severe haemorrhage from this.

Clinical diagnosis: Chorionepithelioma following hydatidiform mole. Treatment was hysterectomy and removal of the vaginal nodule.

Pathological examination.

(1) Hydatidiform mole. This consisted of large masses of vesicular tissue and weighed 1800 g. Histologically, thick large villi with extremely dropsical stroma. Epithelium in certain parts shows excessive proliferation with preponderance of syncytial elements. Where Langhan's cells are seen in great numbers they are surrounded by much fibrin. On some of the villi there are large cushions of well-preserved Langhans' cells. Here and there are necrotic areas.

Diagnosis: Hydatidiform mole with extremely marked epithelial proliferation.

(2) Operation specimen; macroscopic findings: Uterus (7 by 6 by 4 cm.) with adnexae. Surface regular, consistence solid, colour pale yellowish. The surface of the mucosa is very irregular. There

is an elevation, the size of a cherry stone, near the internal os, in which could be seen small vesicles. There is a similar finding at the uterine end of the left Fallopian tube. On the uterus opposite to the first-mentioned elevation there is a small, round, reddish nodule lying partly within the myometrium. The colour of the mucosa varies from greyish yellow to red. The demarcation between the endometrium and myometrium is generally well defined. The myometrium is solid and the vessels clearly distinguished. Sections made through the myometrium in many different planes a few mm. from each other show that there are yellow lines running from the mucosa into the depth of the muscular layer, where they open out into what resembles small honeycombs (Fig. 6). In places these are the size of a cherry and villi can be seen within even by the naked eye. Such formations are to be seen throughout the whole length of the uterus. The Fallopian tubes twisted and a little thickened. Ovaries each the size of a walnut. They contain small cysts which are surrounded by wide yellow borders. The nodule in the vagina measures 2 by 2.5 cm. and is friable.

Microscopic findings: The endometrium in some places appears fairly normal. It is poor in glands but shows some inflammatory infiltration. In other places there are typical puerperal changes such as extensive chorionic invasion, thickening and hyalinization of vessel walls, much inflammation and a little necrosis. However, in many other parts chorionic tissue—villi and epithelium always closely connected—proliferates into the muscular layer. But these proliferations are generally separated from the muscle proper by a wide layer of dense fibrin. Here and there foetal cells are to be seen lying in the vessels. These changes can also be seen in the deeper layers of the endometrium where larger masses of Langhans' cells and syncytial elements are generally found together with the villi or at least having taken their origin from a villus. Haemorrhagic areas are completely absent. The inflammation is less in the deeper layers of the muscle. At each cornu of the uterus very active chorioepithelial proliferation can be seen but without any reaction of the surrounding tissues.

Fallopian tubes: No pathological changes.

Ovaries: Many small cysts in the ovarian stroma containing masses of large luteal cells. Atretic

follicles show wide borders of theca interna cells. In one place there is a ripening follicle with a zone of granulosa cells, but only a few primordial follicles.

Nodule from vagina: Sections consist of old blood, abundant fibrin, lymphocytes and polynuclear leucocytes.*

Mingled with these elements villous stroma without epithelium is frequently seen but in some places villi are seen with well-preserved epithelium. Rarely, degenerating chorionic cell elements are found (Fig. 7).

Diagnosis: Destructive hydatidiform mole with excessive epithelial proliferation and a metastasis in the vagina. The findings do not support the existence of a chorionepithelioma.

DISCUSSION.

It is extremely rare that a placenta with normally shaped villi has such destructive power as that seen in Case 5. Space forbids discussion of this phenomenon and whether it was due to an increased proliferative tendency of the chorionic cells or to a breakdown of the maternal defensive power. This case is described in order to show that enormous destruction may be found even where there is a morphologically unaltered chorionic epithelium. It is common to find a hydatidiform mole that penetrates deeply but it is the extent of the proliferation that varies. Case 6 is a rare one, for it shows a hydatidiform mole *in situ* penetrating deeply into the muscle. So also with Case 7, where an excessive proliferation of the chorionic epithelium and a metastasis in the vagina were found. This combination made diagnosis difficult. To this problem we shall refer later when discussing the subject of malignancy in chorioepithelial proliferations.

* Ladewig's¹⁴ modification of Mallory's stain is a great help since it facilitates the differentiation of tissues even in necrobiosis. This is especially useful when examining material with puerperal changes.

The following facts need to be borne in mind when considering penetration by chorionic elements. The serotina is invaded by chorionic cells. These completely infiltrate the maternal tissues which become compressed and may perish from pressure atrophy. The villi—normally shaped or degenerate—together with the chorionic cells may now penetrate to such a depth that they reach the superficial or even deeper veins of the uterine wall. It is obvious that whole villi or isolated chorionic epithelial cells having reached these veins may find their way into other vessels without difficulty. Their ultimate destination depends on whether or not these cells can still multiply. Epithelial cells of the normal placenta have not this ability. But occasionally they may grow further ahead within the vessels, destroy neighbouring tissues and even break through into other vessels. In this way they cause extremely heavy destruction. Even so this penetration, according to general pathological principles, must still be regarded as a benign one owing to its continuity of growth and its histiotypic form (epithelium and stroma being always together).

Penetration is an attribute of the normal trophoblast and so, in the examination of pathological changes in the chorionic epithelium, one must not attach too much importance to this finding alone. Fig. 4 (Case 6) shows very clearly the thinning of the serotina at one place and villi coming gradually into the most intimate contact with muscle where penetration reaches its maximum. The real destruction in these regions is not as great as would be expected, because the spaces filled with villi and epithelial cells are not the results of a process of liquefaction of the tissues but, in fact, are simply wide veins of the placental site. In some places the walls of the vessels can still be clearly defined. In Case 7 penetration is wider and deeper and is not limited

to the region of the placental insertion. Small fragments of the mole appear close to the peritoneal surface of the uterus and even to the interstitial portions of the Fallopian tubes. That the epithelium of the villi still possesses remarkable proliferative power is proved by the observation that the largest accumulations of chorionic fragments are to be seen at some distance from the cavity of the uterus. As a structural element the epithelium in Case 7 does not play such an important rôle as in Case 6. But chorioepithelial cells may be endowed with considerable destructive power even though there may not be any visible signs of activity (see Case 5, "placenta percreta"). Thus proliferation of chorionic epithelium brings up the recurring question as to when and in what circumstances such proliferation should be regarded as the expression of malignant or benign growth. Most authors who have studied this problem agree that there are some cases in which the above distinction cannot be made by morphological methods alone, although sometimes a careful review and follow-up of a case may eventually lead to its proper interpretation.

Two of the essential characteristics of malignancy—invasion and destruction—are not usually applicable when dealing with the elements of chorionic epithelium. We have already mentioned the similarity between the young trophoblast and chorioepithelioma and have stressed the fact that the main attribute of the chorioepithelioma is its reversion to cytotypic growth. As long as epithelium is found in connexion with villous stroma the morphological proof of its being an independent and cytotypic growth will be extremely difficult, although the possibility of a change from a simple or destructive mole into a chorioepithelioma can never be excluded. However, for diagnosis of malignancy one would insist that the bulk of epithelial

cells should clearly predominate over the stromal, and further, that independent epithelial proliferation should be seen in at least one place. In Case 7 (destructive mole) the tissue as a whole shows signs of exceptionally vigorous proliferation which is less where it has penetrated most deeply. Considerable epithelial proliferation independent of villous stroma was not seen either in the mucosa or in the muscle of the uterus. The way in which the chorioepithelial cells, mostly Langhans' cells, come into contact with muscle resembles closely what is seen in the young trophoblast of extrauterine pregnancy. Meyer⁹ has drawn particular attention to this. In Case 6 (hydatidiform mole *in situ*) there is considerably more epithelial proliferation, and its interpretation depends on the topographical relations of the elements concerned. The anchoring villi of the mole show marked penetrative power. In normal pregnancy villi are commonly found, adjacent to maternal tissue, showing quite thick club-like swellings due to increased proliferation of their cells. It is only to be expected, therefore, that features similar but more striking would be found in cases of hydatidiform mole. These are due to the generally enhanced capacity for growth of the chorioepithelium in this condition. Thus, in this case, there is no doubt that in spite of the strong tendency to proliferation, destruction and infiltration, the only diagnosis that could be considered was that of a benign mole. The features were simply those, but in excess, of the physiological process of nidation.

In Case 7, the significance of the vaginal metastasis remains to be explained. Schmorl¹⁵ was the first to demonstrate that transportation by the bloodstream of whole villi or isolated chorionic cells is almost a feature of normal pregnancy. He has found such cells within the smaller arteries and capillaries of the lungs. In normal preg-

nancy they disappear in a short time. Furthermore in cases of early abortion or hydatidiform mole he has occasionally observed proliferations of displaced chorionic cells growing through the walls of vessels and even infiltrating neighbouring tissues. He explains this phenomenon as due to cell casts of somewhat pathologically altered chorionic epithelium. The elements concerned may go on proliferating for a limited period but will finally be mastered and eliminated by the maternal defence-mechanism. These findings raise the question, in cases of hydatidiform mole with displacement of chorionic cells and their proliferation in other parts of the body, as to whether or not these should be regarded on principle as an expression of malignant growth. There are, of course, numbers of cases cited in which a hydatidiform mole has been followed by metastases showing histologically every sign of a chorionepithelioma. Such a case has been reported by Brews¹⁶ and a similar one will be described later in this paper. On the other hand there are cases where the histology is not so definite. Gygax¹⁷ published a case in which a typical metastasis of a hydatidiform mole was removed from the vulva. There was not any sign of malignant growth in the uterus, and at autopsy (the patient died of an intercurrent illness) all internal organs were free from metastases. Wegelin,¹⁸ too, has demonstrated the benignancy of a metastasis in the vulva, free even of villi, in a case of hydatidiform mole. In this case the histological picture, with regard to the occurrence of isolated cells, fibrin and fibrinoid degeneration, resembles that found during normal placentation in the uterus. The chorionic cells seem actually to be submerged by the masses of fibrin and, as numerous degenerative forms of cell nuclei were to be found, Wegelin concluded that the vulval metastasis in this case must be considered as one

of degeneration which would probably have disappeared without surgical removal. These observations show that the presence of metastases is proof of malignancy only in so far as tumours arising from the individual's own cells are concerned, but in the case of proliferation of foetal cells the above dictum does not necessarily apply. In Case 7, well-preserved and degenerate villi were found but no coherent epithelial cell masses, so one is of the opinion that even the presence of the metastasis does not alter in any way our opinion as to the benignity of the process concerned.

C. CHORIONIC PROLIFERATION WITHOUT VILLOUS STROMA.

Three cases will now be described. The 1st is a typical chorionepithelioma with a metastasis in the vagina, the 2nd is a post-partum chorionepithelioma and the 3rd will be discussed separately as there was an error in diagnosis.

CASE 8. 611/49.

A married woman, aged 17, became pregnant a month after marriage and complained of a brown discharge. At the 4th month there was a haemorrhage and she passed some meat-like tissue. During the following 4 months she was cured 3 times by 3 different doctors. The first curettings were reported to be those of a hydatidiform mole. On arrival at hospital she was suffering from anaemia and on pelvic examination a red swelling the size of a hazelnut was found on the anterior vaginal wall. The rest of the organs were normal. A biopsy of the swelling showed it to be a chorionepithelioma. Hysterectomy was performed. A discharge from hospital 7 weeks later no further nodule was to be found. Seven months later the patient wrote that she was quite well.

Macroscopic findings:

(1) Nodule from vagina, soft, haemorrhagic and friable.

(2) Uterus with adhesion. In the anterior vaginal wall 3 reddish nodules the size of a pea could be palpated easily. Before removal they had been

regular. At the level of the internal os there was another small nodule. The left ovary was cystic. In the left mesovarium there was a dark red, soft nodule of the size of a cherry stone.

Microscopic findings: All the nodules show haemorrhagic necrosis. In several places, especially in the vaginal nodule, numbers of well-preserved Langhans' cells, rare syncytial elements and no villous stroma are to be seen.

Diagnosis: Typical chorionepithelioma with a true metastasis in the vagina.

CASE 9. 247/42.

Married woman, aged 30; 6 full time deliveries and 2 abortions. Patient came to hospital a week after the last delivery complaining of bleeding. Pelvis normal for the period of puerperium. Bleeding ceased and patient discharged; returned to hospital 3 weeks later with severe haemorrhage, very anaemic. The uterus was larger than at examination 4 weeks previously. Curettage was immediately performed. Histological diagnosis, chorionepithelioma. Her condition contra-indicated operation. Twelve days later X-rays showed a normal lung picture. A second X-ray was taken a fortnight later, and showed a shadow the size of a small fist, in the lower lobe of the right lung. She died 14 weeks after delivery. A few days before death there was in the urine a content of 175,000 mouse units per litre of gonadotropic hormone.

Autopsy showed chorionepithelioma of the uterus; multiple metastases of parametrium and both lungs; purulent thrombophlebitis of all pelvic veins up to the vena cava.

Microscopical findings: In many areas of the uterine mucosa there were irregular masses of Langhans' cells and syncytial elements in great number, and these extended into the myometrium causing much destruction of uterine tissue. In the vessels were found elements of the tumour as well as the typical changes of purulent thrombophlebitis. In the lung metastases the tumour was well preserved, there being little necrosis.

DISCUSSION

The vaginal biopsy of Case 8 showed, besides blood and fibrin, large groups of Langhans' cells. The diagnosis of chorion-

epithelioma was obvious. This was confirmed by the case history which showed a clear relation between the hydatidiform mole and the vaginal metastasis. The size of the uterine tumour was unusually small but at the same time it was obviously a typical chorionepithelioma. The repeated curettages may have interfered in some way with the proliferation of the tumour and also the small hormone content of the urine (25,000 mouse units per litre) may be similarly explained. In Case 9 the history was one of postpartum haemorrhage and one would have expected the curettings to have revealed fragments of the placenta or else puerperal endometritis. One would not have expected chorionic epithelium. However, as masses of chorionic epithelial cells, Langhans' and syncytial cells were seen, the diagnosis of chorionepithelioma became obligatory. The subsequent course of the case put the diagnosis beyond all doubt.

CASE 10. 647/41.

Married woman, aged 29; 3 children; 1 year ago induced abortion (4th month). Menstruation usually regular. Last period a fortnight before admission to the hospital. A brisk haemorrhage the night before admission. Haemoglobin 50 per cent (Sahli).

Pelvic examination: Uterus a little larger than normal, external os 1 finger dilated. Curettage performed.

Microscopic findings: Endometrium in secretory phase. Areas of fibrinoid coagulation, and, in contact with these, a tissue consisting of 2 types of cells.

(1) Rather large cells with central nucleus and clear protoplasm arranged in groups (Langhans' cells).

(2) Large confluent elements with varying shapes of nuclei, darkly stained, protoplasm often vacuolated (syncytial elements).

No villous stroma. The syncytial formations are more numerous than Langhans' cells. Three days after curettage the Aschheim-Zondek test with undiluted urine was positive, but was negative in

dilution corresponding to 25,000 mouse units per litre.

A tentative diagnosis of chorionepithelioma was made and the gynaecologist informed that the case should be carefully observed. The gynaecologist decided to perform immediate hysterectomy. A careful histological examination of the specimen showed a perfectly normal uterus. There was no sign of recent pregnancy.

DISCUSSION.

In view of the fact that the uterus did not show the existence of a chorionepithelioma one needs to reconsider the diagnosis which was based on the histological picture of the curettings. Was it possible that the whole of the tumour had been removed by the curettage and that we had been fortunate enough to have seen this? This explanation must be dismissed, since the penetrative power of chorionepithelioma is so great and in the specimen we did not see any penetration into the wall of the uterus. On further reflection it is now obvious that the tissue which we saw in the curettings was not a chorionepithelioma but a simple trophoblast. We were misled because of its highly pleomorphic cellular composition as well as by the complete lack of villi and other puerperal characteristics. We did feel that our diagnosis had to be made with some reserve and at the time informed the gynaecologist of our doubt. However, he was guided by Hirschmann's old dictum that in a doubtful case it is wiser to sacrifice the uterus than to risk the life of the patient.

CONCLUSION.

(1) Isolated chorionic cells *per se* are but an indication of a state of pregnancy either present or past. When large numbers of invading cells are found this usually points to some previous abnormality of the uterus, such as myoma, adenomyosis, or old lesions

—particularly when found a long time after pregnancy—and not to increased, independent activity of trophoblastic derivatives. It always remains with the pathologist, by all the means at his disposal, to establish a relation between chorionic invasion and pregnancy.

(2) The wide range, variations and distribution of cell proliferation and infiltration have been abundantly demonstrated in the above cases. One has purposely selected border-line material in order to emphasize the complexity of the problem and to show the difficulty in reaching a decision as to whether the condition is one of malignant chorionepithelioma or vigorously growing young trophoblast or hydatidiform mole. In these cases the pathologist must of necessity rely on the clinical findings, and especially the history and hormone estimations.

(3) One has attempted to explain that the presence of chorionic cell proliferations in the last month of pregnancy, after a full time delivery, or after an expulsion or removal of a hydatidiform mole supports the diagnosis of malignant chorionepithelioma. When similar histological pictures are present in a still existing mole or early pregnancy then one needs to be most cautious in making the diagnosis of malignancy.

(4) In the same way vaginal metastases are not necessarily malignant. When villous stroma is found in these then one is of the opinion that the condition is innocent.

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The Effect of Postoperative Exercises and Massage on the
Incidence of Pulmonary Embolism at Chelsea
Hospital for Women

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FOR many years the high incidence of pulmonary embolism caused anxiety among the members of the medical staff at Chelsea Hospital for Women. This increased considerably when, in 1936, 50 per cent of the deaths following operations were due to pulmonary emboli.

It was therefore decided at the beginning of 1937 to establish a massage department which was placed under the supervision of one of us (I.C.S.). The duties of the members of the massage team were to instruct and supervise postoperative exercises, and to carry out massage in all cases after abdominal operations and operations for the repair of genital prolapse. The routine following minor operations remained unaltered, and special exercises and massage were not given after such procedures as curettage, insertion of radium, insufflation, etc.

Originally it was intended that the problem be reviewed after 3 years and the incidence of embolism compared in the years preceding and following the introduction of the massage department. Unfortunately the war intervened and detailed study of results was not made. However the experiment was considered a success, as not only did the number of cases of embolism decrease, but the general condition

of the patients on discharge from hospital was obviously greatly improved.

The purpose of this paper is to study the effect of postoperative exercises and massage on the incidence of fatal pulmonary embolism. Non-fatal embolism has not been included as it was found that satisfactory details were not always available in the case notes.

A 14-year period is reviewed and is divided into 2 sections. The first, 1930 to 1936, consists of the 7 years before, and the second, 1937 to 1943, the 7 years after the institution of the massage department.

It is also intended to consider the deaths from embolism collectively and to study such factors as age, type of operation, etc. In addition some details of the type of exercises and massage now being employed at the hospital will be given.

INCIDENCE OF FATAL PULMONARY
EMBOLISM FOLLOWING ABDOMINAL
OPERATIONS.

A. 1930-1936. In this period there were 4,596 abdominal operations followed by 19 deaths from pulmonary embolism, i.e., the mortality from pulmonary embolism was 0.415 per cent or 1 fatal embolism followed every 240.5 abdominal opera-

tions. None of these deaths took place during operation.

B. 1937-1943. In this period there were 3,436 abdominal operations with 9 deaths from pulmonary embolism. In 3 of the 7 years there were no deaths from this cause.

Of the 9 deaths 2 may be excluded for the following reasons. The first, in 1938, took place on the 6th day after operation, but owing to a temporary shortage of staff the patient received no postoperative exercises or massage. The second, in 1943, is excluded as the embolism occurred during the operation.

Excluding these 2 cases the mortality from pulmonary embolism after abdominal operations from 1937 to 1943 was 0.203 per cent, or 1 death followed every 490.5 operations.

The incidence of fatal embolism after abdominal operations was therefore reduced by more than half following the introduction of postoperative exercises and massage.

INCIDENCE OF FATAL PULMONARY EMBOLISM FOLLOWING OPERATIONS FOR THE REPAIR OF GENITAL PROLAPSE.

In each of the 7-year periods there were 2 deaths from pulmonary embolism following roughly equal numbers of operations for prolapse.

Although postoperative exercises and massage have not reduced the number of fatal emboli following these operations, we have been impressed by the marked improvement in muscle tone and posture in this group of patients.

In 1938 Fletcher Shaw and Rickards¹ investigated the incidence of fatal pulmonary embolism after gynaecological operations during a 12-year period at Manchester Royal Infirmary, where exercises are carried out as a routine, and at St. Mary's Hospital, where exercises are not included in the postoperative treatment.

Fatal embolism was found to be 5 times more common in the latter hospital. The authors do not differentiate between abdominal and other operations, and details of the exercises employed are not given.

GENERAL REVIEW.

During the 14-year period 1930 to 1943 there were 21,066 operations at Chelsea Hospital for Women followed by 202 deaths. Of these 202 deaths 40, or 19.8 per cent, resulted from pulmonary embolism, i.e. the incidence of fatal embolism was 0.19 per cent, or 1 such death occurred in every 526 operations. Matas² found that the general prevalence of fatal pulmonary embolism in Europe and America in 2,196,834 operations from 1913 to 1931 was 0.27 per cent or 1 death from embolism in approximately every 500 operations.

According to Henderson³ at the Mayo Clinic during the 10-year period ending in 1927, 6 per cent of all deaths following operation were due to pulmonary embolism. In our series 19.8 per cent of the deaths were due to pulmonary embolism, a much higher figure. This may be due to the fact that a high proportion of the operations (38 per cent) were abdominal.

Of the 40 deaths due to embolism 28, or 70 per cent, followed abdominal operations. Figures from similar series quoted in the recent literature are as follows: Graves,⁴ 65.3 per cent; Henderson,³ 80.7 per cent, Patey,⁵ 86 per cent; Petren,⁶ 88 per cent.

AGE INCIDENCE.

The 40 cases of fatal embolism can be grouped with regard to age as in Table I.

TABLE I.

| Age group | Deaths from embolism |
|----------------|----------------------|
| 20 to 29 years | 2 or 5 per cent |
| 30 to 39 " | 4 or 10 " |
| 40 to 49 " | 11 or 27.5 " |
| 50 to 59 " | 15 or 37.5 " |
| 60 to 69 " | 8 or 20 " |

Five hundred consecutive cases admitted to hospital for operation in 1943 were grouped in a similar way according to age, (Table II).

TABLE II.

| Age group | Percentage |
|----------------|------------|
| 20 to 29 years | 24.4 |
| 30 to 39 " | 37 |
| 40 to 49 " | 22.6 |
| 50 to 59 " | 10.2 |
| 60 to 69 " | 4 |

With the aid of Table II correction was made and an approximate idea of the true incidence according to age was obtained.

From Table III it can be seen that post-operative fatal embolism becomes progressively more common in the higher age groups with a maximal incidence between 60 and 69 years. The average age of the patients was 50.5 years. In Henderson's³ series of 313 fatal cases of embolism the

TABLE III.

| Age group | Corrected incidence |
|----------------|---------------------|
| 20 to 29 years | 1.9 per cent |
| 30 to 39 " | 2.6 " |
| 40 to 49 " | 11.7 " |
| 50 to 59 " | 35.4 " |
| 60 to 69 " | 48.2 " |

average age was 53.2 years and Graves⁴ found that in a series of 194 cases the most common age of occurrence was in the decade 61 to 70 years.

NATURE OF OPERATION.

A. Abdominal operations.

In Table V the abdominal hysterectomies for the two 7-year periods are listed. It is of interest to note the increase in the proportion of total hysterectomies in the 2nd period and the decrease in numbers of the Wertheim operation.

TABLE IV.

| Operation | Number of cases of fatal embolism | | |
|--|-----------------------------------|---------|-------|
| | 1930-36 | 1937-43 | Total |
| Subtotal hysterectomy with or without removal of appendages | 5* | 5 | 10 |
| Total hysterectomy with or without removal of appendages ... | 6 | 1† | 7 |
| Wertheim's hysterectomy | 3 | 0 | 3 |
| Laparotomy for malignant disease | 2 | 1 | 3 |
| Ventral suspension | 1 | 0 | 1 |
| Laparotomy for innocent conditions | 0 | 1 | 1 |
| Myomectomy and ovarian cystectomy | 1 | 0 | 1 |
| Ovariectomy and ventral fixation | 1 | 0 | 1 |
| Repair of ventral hernia | 0 | 1 | 1 |

* In one case perineorrhaphy was also performed.

† Embolism occurred during the operation.

TABLE V.

| Operation | 1930-36 | 1937-43 | Total |
|--|---------|---------|-------|
| Subtotal hysterectomy with or without removal of appendages | 1338 | 930 | 2268 |
| Total hysterectomy with or without removal of appendages ... | 793 | 948 | 1742 |
| Wertheim's hysterectomy | 144 | 61 | 205 |

Incidence of death from pulmonary embolism after:

Subtotal hysterectomy with or without removal of appendages, 0.449 per cent.

Total hysterectomy with or without removal of appendages, 0.401 per cent.

Wertheim's hysterectomy, 1.46 per cent.

There is no marked difference in the incidence of fatal embolism following the subtotal and total operations, but as might be expected it is much higher after Wertheim's hysterectomy.

B. Non-abdominal operations.

In the 14-year period there were 12 deaths from embolism following 13,061 non-abdominal operations or 1 death occurred in every 1,088 operations. It is of interest to note that 4 of the deaths followed the insertion of radium, 3 for malignant disease and 1 for an innocent condition.

NATURE OF DISEASE.

Of the 40 fatal emboli 13 followed operation for malignant disease, 10 abdominal and 3 non-abdominal operations.

TIME OF OCCURRENCE OF PULMONARY EMBOLISM.

Of the 39 emboli which occurred in the postoperative period 17 occurred in the 1st week (all between the 3rd and 7th days), 11 in the 2nd week, 11 in the 3rd, and 1 in the 4th week. The nature of the operation, abdominal or non-abdominal, did not affect materially the time of onset of the embolism. Thus following abdominal operations there were 10 deaths in the 1st week, 7 in the 2nd, 9 in the 3rd, and 1 in the 4th week.

PRESENCE OF PYREXIA PRECEDING EMBOLISM.

In a series of 146 fatal cases Robertson⁷ found unexplained moderate fever in 18 per cent during the postoperative period. In

our series of 40, only 32 temperature charts were still available. In 25 of these, or 78.1 per cent, some elevation of temperature was present during the 3 days immediately preceding the fatal embolism. This generally took the form of a mild intermittent pyrexia ranging from 99 to 100.5° F.

BRIEF OUTLINE OF THE EXERCISES AND MASSAGE EMPLOYED.

The main aims of treatment are as follows:

1. Increased respiratory excursion resulting in improved venous return to the heart.

2. Improvement of the circulation and maintenance of muscle tone in the limbs.

3. Strengthening of the abdominal and perineal muscles and later the development of correct posture.

Abdominal operations.

The patient receives instruction in breathing exercises on the day before operation. These are commenced on the day following operation and she is encouraged to carry out active foot exercises; namely bending, stretching and rolling of the foot. On the 3rd day quadriceps contractions, gluteal contractions and more extensive foot movements are added and gentle massage of the legs is begun.

After the abdominal clips have been removed abdominal and gluteal contractions are introduced, and adduction exercises to improve the tone of the muscles of the pelvic floor.

Later the exercises are carried out with the patient's legs over the side of the bed, and trunk rotation, flexion and extension are begun. Eventually the standing position is adopted during the exercises and care is taken that the correct posture is being achieved. The patient leaves hospital with instructions to continue the exercises at home for at least a further 2 weeks.

Operations for the Repair of Prolapse.

A similar routine is employed, but perineal exercises are not introduced until after the 10th day to avoid unnecessary discomfort from stitches.

DISCUSSION.

Much useful work has been carried out in recent years in an attempt to discover the aetiology of postoperative thrombosis and embolism. Perhaps the most productive has been the investigation of the constituents of the blood, particularly those taking part in the process of coagulation. Among others Atkins⁶ has shown that there is a fall in the platelet count after operation followed by a sharp rise beginning on the 7th day and reaching a maximum about the 10th day. Robertson⁷ found that the coagulation time was shortened and the sedimentation-rate increased. As these changes take place after every operation it is unlikely that they are the only factors leading to embolism.

Infection may play a part, and we have shown that in 78 per cent of our fatal cases some elevation of temperature was present during the 3 days preceding the embolism. As both Robertson⁷ and Bonney⁹ have pointed out, frank thrombophlebitis rarely precedes pulmonary embolism since the clot then is so adherent to the inflamed vessel wall that it cannot readily break loose. The infection is therefore probably of a mild type, insufficient in itself to produce an obvious phlebitis, yet of some importance in the production of thrombosis and embolism.

Most authorities are agreed that one of the principal contributory factor is venous stasis. This results from the relatively immobile position of the patient in bed, from obstruction such as that produced by the

knee pillow and from diminished respiratory excursion. The venous return to the heart is dependent largely on the negative pressure in the thorax during inspiration and, at the same time, on the increased abdominal pressure resulting from descent of the diaphragm. In the limbs contraction of the muscles encourages movement of the blood in the veins.

In the past various types of prophylactic treatment have been suggested, many directed against the changes in the constituents of the blood. Thyroid extract, a diet low in fat and proteins, and anticoagulants such as heparin have been used with varying success. The most profitable lines of treatment however have been those directed to combating venous stasis. The simple expedient of raising the foot of the bed several times daily may be of some value, but we are of the opinion that stasis can best be prevented by active exercises and massage. Breathing exercises, abdominal massage and pressure applied particularly during inspiration, and active movements of the limbs encourage venous return to the heart. These should be commenced as soon as possible after operation, as in our series 43.5 per cent of the cases of fatal embolism occurred in the 1st week.

At Chelsea Hospital those who have undergone abdominal operations or operations for the repair of prolapse are the only patients who receive the benefits of postoperative exercises and massage. We believe that these could be extended advantageously to selected cases after minor procedures. We agree with Snell¹⁰ who says "It is probable that there is a group of patients over 50 years of age, obese and with a normal or subnormal blood-pressure, who are particularly susceptible to pulmonary embolism as a postoperative complication," and we would add that this is even more likely in the presence of malignant pelvic disease.

SUMMARY.

Postoperative exercises and massage were introduced at Chelsea Hospital for Women in 1937 in an attempt to reduce the incidence of pulmonary embolism.

The incidence of fatal embolism following abdominal operations fell by more than 50 per cent in the subsequent 7-year period.

The deaths from embolism are reviewed with regard to general incidence, age of patient, type of operation, etc.

Some details of the exercises and massage employed are given and are followed by a short discussion with references to recent literature.

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A Short Study of Histaminase Activity During Pregnancy

BY

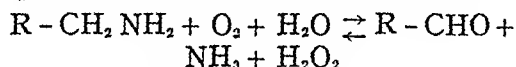
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INTRODUCTION.

Histaminase, first described by Best and McHenry¹ is an enzyme which inactivates histamine.

Its action, according to Zeller,² might be represented by the following equation:



where R is an iminazole ring.

In support of this view Stephenson³ has shown that during the activity of histaminase, oxygen is consumed and that ammonia and hydrogen peroxide are liberated. Laskowski⁴ found that the amount of oxygen utilized throughout this process depends on the purity of histaminase. Among impurities affecting the enzyme haemin accelerates its activity.

There is a disagreement as to the specificity of histaminase activity. On the one hand there is a group of authors that believes it to be specific. This view was first suggested by its originators, Best and McHenry,¹ who distinguished histaminase from tyramine-oxidase. Blaschko, Richter and Schlossman⁵ showed that adrenaline, aliphatic amine and tyramine oxidases are substantially similar, whereas histaminase differed greatly from them. Kapeller-Adler,⁶ in one of her last works, demonstrated the difference between specific histamine-histaminase reaction and another non-specific deamination of cadaverine. Blaschko⁷ showed that cadaverine and histamine had no affinity to amino-oxidase.

On the other hand, another group of authors regarded the reaction as non-specific and supposed it to be equally effective against deamines such as cadaverine and spermin. Thus Zeller, Wenk and Stern,⁸ and Zeller⁹ believed histaminase to be identical with deamino-oxidase and claimed also that the former produced the deamination of putrescin and agmatin.

According to Werle and Effkeman¹⁰ and Kapeller-Adler⁶ histaminase reaction is specific with regard to histamine and can only be demonstrated in serum from the pregnant woman.

There is a difference in the action of histaminase *in vivo* from that *in vitro* which was emphasized by Atkinson and Ivy.¹¹ Investigations *in vitro* by Kapeller-Adler⁶ showed that histaminase activity was impaired in the cases of pre-eclampsia and completely inhibited by addition of aneurin.

The purpose of the present investigations was fourfold:

- (1) To assess the specificity of histaminase.
- (2) To estimate the activity of histaminase in non-pregnant sera.
- (3) To study the fluctuation of histaminase in the course of pregnancy.
- (4) To examine factors inhibiting the activity of histaminase.

METHOD.

One method of measuring the activity of histaminase employed for deamino-oxidase

and applied lately for histaminase is based upon the decolorization of indigo disulphonate presumably by hydrogen peroxide. This is the basis of the method used by Kapeller-Adler. From the degree of decolorization the activity of enzyme is estimated. Briefly the method involves the mixture of serum, histamine (cadaverine) and dye, followed by a study of colour changes. The details were as follows:

Reagents:

Solutions of:

M/15 phosphate buffer (Sorensen) $pH=7.2$

M/20 histamine hydrochloride in M/15 phosphate buffer.

M/20 cadaverine hydrochloride in M/15 phosphate buffer.

200 mgms. of indigo disulphonate in 300 ml. of phosphate buffer.

The latter solution when kept in darkness for a fortnight is stable and meets the requirement of logarithmic line of the photo-electric colorimeter.

Saturated ammonia sulphate.

Acetone.

Preparation of the sera:

The sera were dialysed against the phosphate buffer in a refrigerator for 12 hours. To ensure similar conditions in all the experiments, only non-haemolysed sera were used and the dialysers made in the same manner from the same material; similarly the same amount of buffer was taken for each dialysis.

To 1 ml. of dialysed serum 0.2 ml. of M/20 histamine, 0.2 ml. of dye solutions and 0.1 ml. of toluene were added. The tubes with cadaverine were similarly arranged.

Two control tubes were introduced in each of which 0.2 ml. of phosphate buffer (instead of histamine or cadaverine) was added; otherwise the compounds were the same.

Air was sucked through the mixture in each of the 3 tubes for 5 minutes. One of the two control tubes and a histamine (cada-

verine) tube were set in the incubator for 72 hours at $37^{\circ}C$. The second control tube was put in boiling water for 2 minutes in order to stop enzyme activity, thus preventing the decolorization by histaminase.

At this juncture it seems appropriate to draw attention to 4 modifications that have been made to the original Kapeller-Adler method.

1. According to Kapeller-Adler, after 24 hours a comparison between control tube 1 and histamine tube is made thus: - = no decolorization; + = slight; ++ = distinct; +++ = complete decolorization. In the present work this was modified by the addition of group \pm because the distinction between minus and one plus decolorization was found difficult.

2. Air was used instead of oxygen.

3. It was found difficult to differentiate distinctly the degree of decolorization especially with the sera of early weeks of pregnancy. Therefore the time of incubation was extended to 72 hours and 12 sera were carefully studied to show the difference between 24 and 72 hourly investigations.

In Table I the results of this study are recorded. It can be seen that the 72 hours incubations gave more satisfactory results and that the decolorization of the dye in the presence of histamine as compared with cadaverine was more pronounced. Because of this histamine was chosen as a substrate and all further readings were made after 72 hours.

4. In spite of these alterations it was still difficult, because of the varying colour shades, to distinguish the degree of decolorization; this was especially noticeable in the groups labelled 'minus' and 'one plus' decolorization. To overcome these difficulties the fourth modification was introduced and an extract of dye (see below) with acetone and saturated ammonium sulphate was made. The degree of decoloriza-

was carried out in order to obtain estimates of specific histaminase and non-specific activity of serum within the group of normal non-pregnant women.

It was often found with the sera of non-pregnant women, some of which had to be discarded because of uncertainty about the women's clinical state, that addition of histaminase accelerated the decolorization in one case but retarded it in another. It should be noticed in the recorded results that on 5 out of 12 occasions the values of histaminase activities were negative and

no evidence of specific histaminase activity but clear evidence of non-specific activity of serum.

Changes in histaminase and non-specific activity of serum during the course of pregnancy.

The present investigations were chiefly concerned with the fluctuations of histaminase during pregnancy. The patients were chosen when the date of the last menstrual period was known so that it was possible to calculate duration of pregnancy in days.

TABLE III.

Estimation of "specific histaminase" and "non-specific" activities in sera from non-pregnant women.

Mgm. of dye per 1 ml. of serum.

| No. of investigation | Modified Kapeller-Adler estimation | I Control | Histamine | II Control | Specific histaminase activity | Non-specific activity of serum |
|----------------------|------------------------------------|-----------|-----------|------------|-------------------------------|--------------------------------|
| 160 | - to \pm | 0.022 | 0.033 | 0.022 | 0.011 | 0.000 |
| 167 | - to \pm | 0.050 | 0.040 | 0.027 | -0.010 | 0.023 |
| 169 | - to \pm | 0.048 | 0.040 | 0.028 | -0.008 | 0.020 |
| 170 | - to \pm | 0.053 | 0.033 | 0.038 | -0.020 | 0.015 |
| 181 | - to \pm | 0.040 | 0.042 | 0.038 | 0.002 | 0.002 |
| 186 | - to \pm | 0.052 | 0.053 | 0.022 | 0.001 | 0.030 |
| 195 | - to \pm | 0.033 | 0.042 | 0.019 | 0.009 | 0.014 |
| 196 | - to \pm | 0.042 | 0.033 | 0.020 | -0.009 | 0.022 |
| 200 | - to \pm | 0.047 | 0.042 | 0.042 | -0.005 | 0.005 |
| 217 | - to \pm | 0.042 | 0.045 | 0.042 | 0.003 | 0.000 |
| 218 | - to \pm | 0.028 | 0.047 | 0.022 | 0.019 | 0.006 |
| 219 | - to \pm | 0.031 | 0.043 | 0.022 | 0.012 | 0.009 |

on the remaining 7 occasions it was positive; the average was, however, very low (0.0004167, standard error \pm 0.003243) and by a recognized test (Fisher¹²) was not significantly different from zero (P approximately 0.9).

In contrast, on all 12 occasions the values for non-specific activity of serum were positive and the mean (0.012167, standard error \pm 0.002892) was significantly different from zero ($P < 0.01$).

It could be said, therefore, that in the group of 12 non-pregnant women there was

A preliminary survey of the columns of specific histaminase activity shows a general tendency to a greater degree of decolorization of indigo disulphonate as the pregnancy advances; it could be noticed in both the qualitative and quantitative columns (2 and 6 of Table IV).

The data were subdivided into groups of equal time interval (25 days) and the average specific histaminase activity (\bar{x} = mgm. of decolorized dye $\times 10^3$) for each group was calculated together with the average duration of pregnancy in days (\bar{t}).

TABLE IV.
Estimation of histaminase activity. Normal pregnant sera.
 Mg. of dye per 1 ml. of serum.

| No. of investigation | Modified Kapeller-Adler estimation | I Control | Histamine | II Control | Specific histaminase activity | Non-specific activity of serum | Days of pregnancy |
|----------------------|------------------------------------|-----------|-----------|------------|-------------------------------|--------------------------------|-------------------|
| 153 | — | 0.055 | 0.045 | 0.043 | —0.010 | 0.012 | 57 |
| 124 | + | 0.055 | 0.050 | 0.045 | —0.005 | 0.010 | 63 |
| 132 | — | 0.045 | 0.045 | 0.027 | 0.000 | 0.018 | 63 |
| 183 | — | 0.047 | 0.047 | 0.022 | 0.000 | 0.025 | 65 |
| 122 | + | 0.047 | 0.067 | 0.030 | 0.020 | 0.017 | 66 |
| 204 | ± | 0.067 | 0.083 | 0.019 | 0.016 | 0.048 | 73 |
| 189 | + | 0.036 | 0.057 | 0.036 | 0.021 | 0.000 | 75 |
| 172 | ± | 0.047 | 0.057 | 0.022 | 0.010 | 0.025 | 76 |
| 194 | ++ | 0.045 | 0.081 | 0.031 | 0.036 | 0.014 | 78 |
| 163 | — | 0.045 | 0.045 | 0.022 | 0.000 | 0.023 | 78 |
| 149 | + | 0.055 | 0.060 | 0.040 | 0.005 | 0.015 | 79 |
| 157 | — | 0.055 | 0.059 | 0.052 | 0.004 | 0.003 | 79 |
| 188 | + | 0.045 | 0.060 | 0.027 | 0.015 | 0.018 | 79 |
| 155 | ++ | 0.060 | 0.085 | 0.060 | 0.015 | 0.000 | 81 |
| 129 | + | 0.042 | 0.050 | 0.028 | 0.008 | 0.014 | 82 |
| 158 | + | 0.052 | 0.062 | 0.043 | 0.010 | 0.009 | 82 |
| 179 | ± | 0.055 | 0.077 | 0.028 | 0.022 | 0.027 | 84 |
| 180 | ± | 0.045 | 0.060 | 0.027 | 0.015 | 0.018 | 84 |
| 205 | ± | 0.078 | 0.075 | 0.022 | —0.003 | 0.056 | 85 |
| 177 | ± | 0.050 | 0.072 | 0.027 | 0.022 | 0.023 | 87 |
| 211 | ++ | 0.040 | 0.057 | 0.036 | 0.017 | 0.004 | 88 |
| 99 | + | 0.033 | 0.055 | 0.028 | 0.022 | 0.005 | 94 |
| 207 | + | 0.060 | 0.093 | 0.020 | 0.033 | 0.040 | 95 |
| 137 | ++ | 0.062 | 0.072 | 0.062 | 0.010 | 0.000 | 97 |
| 152 | — | 0.052 | 0.050 | 0.042 | —0.002 | 0.010 | 97 |
| 125 | + | 0.053 | 0.070 | 0.048 | 0.017 | 0.005 | 99 |
| 161 | ++ | 0.022 | 0.067 | 0.022 | 0.045 | 0.000 | 100 |
| 174 | ++ | 0.047 | 0.075 | 0.031 | 0.028 | 0.016 | 103 |
| 139 | ++ | 0.050 | 0.067 | 0.043 | 0.017 | 0.007 | 105 |
| 162 | + | 0.027 | 0.045 | 0.017 | 0.018 | 0.010 | 117 |
| 191 | + | 0.040 | 0.070 | 0.019 | 0.030 | 0.021 | 120 |
| 130 | ++ | 0.045 | 0.055 | 0.030 | 0.020 | 0.015 | 121 |
| 184 | +++ | 0.033 | 0.115 | 0.020 | 0.082 | 0.013 | 133 |
| 209 | ++ | 0.050 | 0.093 | 0.020 | 0.043 | 0.030 | 139 |
| 154 | + | 0.052 | 0.072 | 0.028 | 0.020 | 0.024 | 152 |
| 175 | ++ | 0.022 | 0.065 | 0.017 | 0.043 | 0.005 | 158 |
| 178 | +++ | 0.047 | 0.117 | 0.047 | 0.070 | 0.000 | 176 |
| 128 | +++ | 0.042 | 0.083 | 0.027 | 0.041 | 0.015 | 182 |
| 173 | +++ | 0.048 | 0.103 | 0.022 | 0.055 | 0.026 | 242 |
| 146 | ++ | 0.073 | 0.123 | 0.040 | 0.050 | 0.033 | 243 |

By the analysis of variance it was found that the variability between groups could not be explained by the variability within groups ($P < 0.001$), so there can be no doubt that specific histaminase activity changes as the pregnancy advances.

The next point to be considered is the nature of the change in specific histaminase activity with advancing pregnancy. Inspection of Table IVa shows that the means of \bar{x} are low in the first 100 days, thereafter rising considerably. Further

TABLE IVa.

Correlation table of the mean specific histaminase activity $\times 10^3$ with the mean duration of pregnancy in 8 periods of gestation.

| No. of observations | Days | \bar{x} | \bar{t} |
|---------------------|------|-----------|-----------|
| 6 | 50 | 3.5 | 64 |
| 20 | 75 | 13.85 | 85 |
| 6 | 100 | 26.33 | 111 |
| 2 | 125 | 62.5 | 136 |
| 2 | 150 | 31.5 | 155 |
| 2 | 175 | 55.5 | 179 |
| — | 200 | — | — |
| 2 | 225 | 52.5 | 242 |

Analysis of Variance.

| | Between groups | Within groups | Total |
|--------------------|----------------|---------------|----------|
| Sum of squares | 11050.61 | 4839.39 | 15890.00 |
| Degrees of freedom | 6 | 33 | 39 |
| Mean square | 1841.77 | 146.65 | |
| Variance ratio | 12.6 | | |
| Probability | $P < 0.001$ | | |

analysis by the above technique showed that a straight line was not a good expression of the change. In view of the fact that there were comparatively few observations in the last few weeks of gestation the precise nature of the curve representing the change in specific histaminase activity with advancing pregnancy cannot as yet be settled. Further studies on the nature of the curve are required.

The non-specific activity of serum was similarly analyzed.

It is clear that the variability within and between groups is very similar so there is no evidence that non-specific activity of serum changes with advancing pregnancy.

TABLE IVb.
Analysis of variance.

| | Between groups | Within groups | Total |
|--------------------|----------------|---------------|--------|
| Sum of squares | 889.32 | 5603.78 | 6493.1 |
| Degrees of freedom | 6 | 33 | 39 |
| Mean square | 148.22 | 169.81 | |
| Variance ratio | 1.15 | | |
| Probability | $P > 0.2$ | | |

FACTORS POSSIBLY MODIFYING THE ACTIVITY OF HISTAMINASE.

A. *Pre-eclamptic sera.*

The sera from 9 cases of pre-eclampsia were studied as regards specific and non-specific activity of serum. In Table V the results are recorded.

It could be seen that the average duration of pregnancy in this group was longer than in our group of normal pregnant sera, so a comparison could not reasonably be made.

The means of specific histaminase activity (0.03333, standard error ± 0.00557) and non-specific activity of serum (0.02867, standard error ± 0.00575) were both significantly different from zero ($P < 0.001$). The following guarded conclusions may therefore be drawn: pre-eclampsia does not stop histaminase or non-specific activity of serum. It is not, however, possible to say whether or not it lessens such activities.

B. *Histaminase and aneurin.*

Table VI presents the results from adding aneurin in the proportion of 5 mg. to 1 ml. of serum to the sera from 4 pregnant women. Sufficient serum for parallel investigations on individual samples was not available and the comparison was, therefore, made with

TABLE V.
Estimation of histaminase activity. Pre-eclamptic sera.
 Mg. of dye per 1 ml. of serum.

| No. of investigation | Modified Kapeller-Adler estimation | I Control | Histamine | II Control | Specific histaminase activity | Non-specific activity of serum | Weeks of pregnancy |
|----------------------|------------------------------------|-----------|-----------|------------|-------------------------------|--------------------------------|--------------------|
| 140 | ++ | 0.055 | 0.077 | 0.042 | 0.022 | 0.013 | 33 |
| 141 | + | 0.085 | 0.100 | 0.050 | 0.015 | 0.035 | 37 |
| 142 | +++ | 0.057 | 0.105 | 0.017 | 0.048 | 0.040 | 34 |
| 143 | ++ | 0.053 | 0.102 | 0.027 | 0.049 | 0.026 | 39 |
| 144 | + | 0.052 | 0.057 | 0.020 | 0.005 | 0.032 | 38 |
| 145 | + | 0.073 | 0.105 | 0.023 | 0.032 | 0.050 | 29 |
| 159 | ++ | 0.031 | 0.075 | 0.027 | 0.044 | 0.004 | 37 |
| 176 | ++ | 0.038 | 0.070 | 0.030 | 0.032 | 0.008 | 37 |
| 197 | ++ | 0.070 | 0.123 | 0.020 | 0.053 | 0.050 | 36 |

TABLE VI.
Estimation of specific histaminase and non-specific activity of serum.
 Mg. of dye per 1 ml. of serum. Addition of aneurin.

| No. of investigation | Modified Kapeller-Adler estimation | I Control | Histamine | II Control | Specific histaminase activity | Non-specific activity of serum | Days of pregnancy |
|----------------------|------------------------------------|-----------|-----------|------------|-------------------------------|--------------------------------|-------------------|
| 212 | — | 0.085 | 0.090 | 0.030 | 0.005 | 0.055 | 89 |
| 213 | — | 0.083 | 0.085 | 0.062 | 0.002 | 0.021 | 96 |
| 214 | — to ± | 0.060 | 0.072 | 0.030 | 0.012 | 0.030 | 92 |
| 215 | — | 0.059 | 0.064 | 0.022 | 0.005 | 0.037 | 54 |

the first 26 cases of the pregnant group. In both the former and the latter series the range of duration of gestation varied between 50 and 100 days.

Qualitative estimation of sera to which aneurin was added gave negative results in 3 cases and a doubtful result in 1. Corresponding readings for sera in the group of normal pregnancies (Nos. 153 to 125, Table IV) varied between — to ++.

When the difference of the means of specific histaminase activities in the 2 groups was studied, it was found to amount to only 0.93 ($P > 0.3$) times its standard error. In contrast, the difference between the means of non-specific activity of serum was 2.47 ($P = 0.02$) times its standard error. In each comparison the degrees of freedom were 28.

From this analysis it could be seen that there was no clear evidence that the addition of aneurin inhibits or accelerates specific histaminase activity. The data, however, suggest that aneurin or its degradation products may accelerate non-specific activity of the serum, though the series is so small that there could be no certainty on this matter. Further investigations are required to give unequivocal results.

DISCUSSION.

This investigation presents a method for the quantitative estimation of serum histaminase which, it is hoped, will prove useful in following more precisely the changes in the amount of the enzyme during the course of normal and abnormal pregnancy.

The method was worked out from

Kapeller-Adler's test based upon a qualitative method in which H_2O_2 produced by the action of histaminase upon histamine decolorizes the dye indigo disulphonate. To this method three modifications were introduced.

1. Air was used instead of oxygen.
2. The time of incubation was extended to 72 hours.
3. The degree of decolorization was measured by an Evelyn photo-electric colorimeter (instead of naked eye distinction of Kapeller-Adler) and expressed in milligrams of dye per 1 ml. of serum.

It was found that there were 3 groups of factors responsible for the decolorization of dye. Firstly, the effect of mixing dye and serum; secondly, the non-specific activity of serum brought to light by incubation; thirdly, the specific histaminase activity resulting from the further addition of histamine. For each sample of serum 3 separate tubes were set up and studied: they were as follows: (1) serum and dye were mixed and boiled for 2 minutes to stop enzyme activity. This was called control tube II. (2) Serum and dye were mixed and incubated at $37^\circ C$. for 72 hours. This was called control tube I. (3) Serum, dye and histamine were mixed and incubated. This was called histamine tube.

In each case the decolorization was measured and expressed in mg. of dye per 1 ml. of serum. The difference between the first control tube and the second control tube is the measure of the effect of incubation upon the serum; this was arbitrarily called "non-specific activity" of the serum. This decolorization may be attributed to enzymatic reaction or oxidants present in the serum. Nevertheless there would seem to be some substances in plasma which contribute to the decolorization of indigo disulphonate and of which

due account must be taken in determining the histaminase activity of plasma.

Altogether serum from 12 non-pregnant, 40 normal pregnant, and 9 pre-eclamptic pregnant women were available for this study. There was also pooled serum from pregnant women upon which the effect of adding aneurin was studied.

From the investigations upon the serum obtained from non-pregnant women there was no evidence of specific histaminase activity; but there was definite non-specific activity in the serum. The underlying explanation of the latter observation is obscure.

When, however, the serum from the normal pregnant woman was studied, there was definite evidence of specific histaminase activity. Furthermore, the activity varied with the duration of pregnancy. Thus, it was low in the first 100 days and high thereafter. These findings agree with those of others (Werle and Effkemann," Kapeller-Adler⁶). Statistical analysis showed that the straight line was not a good expression of the change of this activity with advancing pregnancy. Until further cases are studied the precise nature of this change cannot be settled. The elaboration of an amine-oxidase within the body during pregnancy constitutes an interesting problem which quantitative measurement will assist in solving.

The sera from patients with pre-eclampsia showed also histaminase activity. Comparison of these findings with those of Kapeller-Adler is not easy since our data were not extensive. So far as the material allowed, it was impossible to demonstrate the inhibition of either histaminase or non-specific activities of serum.

The serum from non-pregnant and pregnant women showed roughly the same amount of non-specific activity. Furthermore, during pregnancy its amount does not change.

It was also possible to confirm Kapeller-Adler's finding that serum produces a greater degree of decolorization with histamine as a substrate than with cadaverine. A real explanation cannot yet be produced for this difference. It may represent a difference in rates of the same enzymatic reaction or be due to the presence of two enzymes.

The study of the pooled sera to which aneurin was added did not show any clear evidence that inhibition of specific histaminase activity takes place. In contrast, the data suggest that aneurin may accelerate non-specific activity of serum. Further studies on that subject are required.

It is hoped in further investigations to elaborate the function of histaminase in pregnancy. This enzyme may be an important link in the metabolism of histidine during pregnancy.

SUMMARY.

1. The ability of serum to decolorize indigo disulphonate has been studied in 12 non-pregnant, 40 pregnant and 9 pre-eclamptic women.

2. Two important factors influenced the decolorization:

(1) Non-specific activity associated with incubation.

(2) Specific histaminase activity associated with incubation and the presence of histamine in the serum-dye mixture.

3. The evidence is presented of the existence of similar non-specific activity in sera of all three groups.

4. There was no evidence of specific histamine activity in serum from non-pregnant women.

5. There was clear evidence of specific histaminase activity in the last 6 months of pregnancy.

6. Serum from pre-eclamptic women still shows specific histaminase activity.

7. The addition of aneurin to pooled serum does not materially alter either non-specific activity or specific histaminase activity of serum though there is a faint suggestion that it may increase the non-specific activity.

8. The significance of these results has been briefly discussed.

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Acute Hydramnios

(A Brief Survey of the Recent Literature, with Report of a Case Simulating Concealed Accidental Haemorrhage)

BY

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ACUTE hydramnios is such a rare condition that F. J. Browne¹ recommends that every case should be reported. Chambrelent² found only 50 cases reported in the literature up to 1914, and a survey of subsequent literature reveals only a further 40 cases, making a total of 90 cases in all.

AETIOLOGY.

The cause of acute hydramnios is still unknown, and is likely to remain so until more light is shed upon the origin of the amniotic fluid and the factors which regulate the rate and amount of its secretion. Many theories of causation of the chronic variety have been advanced, and many indisputable facts have been brought forward in their support, but none of them explains why a large amount of fluid should suddenly accumulate in the amniotic sac in a matter of hours.

The amniotic fluid is generally regarded as of dual origin, being contributed both by the mother and by the products of conception. On the maternal side the fluid comes from the blood plasma, and is probably changed by its passage across placenta and amnion. The work of Polano,³ Keiffer,⁴ and Goldman⁵ proved that the amnion is capable of true secretory activity.

The foetus probably contributes by urinary secretion (Acosta-Sison⁶) and by transudation from the foetal surface and umbilical cord. Under normal conditions

the foetus also probably helps to regulate the amount by constant swallowing of liquor and the subsequent passage of excess fluid into the foetal circulation and across the placenta into the maternal blood-stream (Tauszig⁷).

In hydramnios, therefore, pathological conditions, both on the maternal and on the foetal side (including chorion, amnion and umbilical cord), may be contributory if not sole causes of the condition.

Analysis of the 40 cases of acute hydramnios reported in the literature since 1914 reveals the following facts:

Eight cases were associated with twin pregnancy (Garipuy and Guilhem,⁸ Matera⁹ 3 cases, Gaetgens,¹⁰ Houlton,¹¹ Haro Garcia,¹² Audebert and Ribat¹³). In the case reported by Audebert and Ribat there was an acute accumulation of excess of liquor in both amniotic sacs. In 7 cases the foetus was anencephalic (Cornell¹⁴ 5 cases, Payne and Bland¹⁵ 2 cases). In the two latter cases the patients had had several previous unsuccessful pregnancies which had terminated spontaneously in the early months. Two cases were associated with teratoma of the neck (Wilson¹⁶).

Other foetal deformities occurring singly were: Multiple deformities (Garipuy and Guilhem⁸), atresia of the oesophagus (Fukas¹⁷), congenital adenoma of the lung (Esch¹⁸), hydrocephalic anophthalmic monster (Tillim¹⁹).

Maternal associated conditions found were: Ascariasis, appearing acutely in the puerperium (Lanfranchi²⁰), diabetes mellitus, with recovery of both mother and child (Voron and Gaucheraud²¹).

Eclampsia—this case, like the author's, was erroneously diagnosed as premature separation of the placenta (Calatuzzolo²²).

CASE REPORT.

Mrs. E. W., a primigravida, aged 23 years, first attended the antenatal clinic on November 27th, 1944. Her personal and family history and the history of the pregnancy were satisfactory. The previous menstrual rhythm was regular (4/28); the last menstrual period was on May 23rd, 1944, and the expected date of delivery was March 2nd, 1945. General physical examination showed a healthy, normal young woman (weight 9 stone, 6 pounds, blood-pressure 110/70; urine, sugar- and albumin-free). The abdomen contained a central tumour corresponding to the period of amenorrhoea, with palpable foetal parts and audible foetal heart. The presentation was "vertex," and the external measurements normal; vaginal examination revealed a roomy pelvis. The Wassermann reaction was negative.

She attended the clinic again on December 18th, 1944, and was then feeling very well. She felt active foetal movements, the uterus corresponded in size to a pregnancy of 28 to 30 weeks, and the urine was albumin-free. She was told to report again for examination in two weeks.

On December 23rd, 1944, at 3.30 a.m., she was admitted to the maternity department complaining of extremely severe abdominal pain, which she said had begun suddenly on the previous evening, with vomiting. Only when the diagnosis had been established and she was closely questioned, did she admit having had vague abdominal discomfort since the previous day. The pain was constant and aching in character, and unvarying in intensity, and it was so severe that the patient retired to bed. As it persisted and she was unable to rest, she called an ambulance for admission to hospital.

On admission she looked pale and shocked and was obviously in great pain. The abdomen was extremely tense, hard and tender; occasional pain-

less contractions were palpable. Foetal parts could not be felt and the foetal heart was inaudible. The patient volunteered the information that she had not felt any movements since the previous day. The fundus uteri reached up to about 2 inches below the xiphisternum. There was no vaginal bleeding. External ballottement could not be elicited and rectal examination revealed that the cervix was closed and not taken up. The blood-pressure was 150/90; the pulse was of poor volume and the rate averaged 150 per minute. Four ounces of urine were recovered by catheterization; it was sugar- and albumin-free.

Owing to the suddenness of onset of the pain, the hard, tense, tender abdomen, the hypertension and the poor general condition of the patient, a diagnosis of concealed accidental haemorrhage was made. Morphia gr. $\frac{1}{4}$ was administered, the blood was grouped and serum for cross-typing was obtained. The height of the fundus was marked, and the patient kept under constant supervision. At 9.30 a.m. there was no evidence of the onset of labour and the general condition of the patient was no better. The abdomen had not enlarged further but she was still vomiting. Vaginal examination revealed a closed cervix, but tense, bulging, intact membranes could be felt with the finger-tip; there was no other palpable abnormality. At this stage it was decided to try and start labour with pituitrin and stilboestrol. After 4 half-hourly doses of 0.25 c.cm. pituitrin with 5 mg. stilboestrol, pains commenced and the membranes were ruptured with a Spencer Wells forceps. It was then noticed, with considerable surprise, that the liquor was under great tension; it shot out to a distance of about 6 inches beyond the vulva. It maintained this pressure until a total of 5 pints had been collected; a further pint trickled out. The liquor was clean and normal in appearance. It now became evident that the diagnosis of concealed accidental haemorrhage was erroneous; it was a case of acute hydramnios.

The level of the uterine fundus sank down to the umbilicus and there was an instantaneous improvement in the patient's condition; she expressed great relief. The blood-pressure, which was recorded immediately afterwards, was 120/80. By vaginal examination after rupture of the membranes it was possible to feel an ear presenting; the occiput was not palpable and it was concluded

REVIEW OF HOSPITAL REPORT

THE CLINICAL REPORT OF THE NATIONAL MATERNITY HOSPITAL, DUBLIN, FOR THE YEAR 1944.

DURING the year there were 3,858 patients admitted to the maternity wards of the hospital. There resulted from these 3,187 intern-deliveries. This is an increase of 168 admissions and 185 deliveries on the previous year's figures. The result, according to the Master, is an overloading of the intern maternity service with the resultant evils of the shortened puerperium and incomplete establishment of breast feeding. As the number of beds in the maternity department is not stated it is not possible to estimate just how serious the overcrowding is.

In the first 17 pages there is a summary of the most important features of the report. The next 73 pages are concerned with detail. Here many conditions are set out case by case while others (e.g. breech delivery and delivery by the forceps) are summarized numerically in tabular form. Why these conditions should be selected for compression is not made clear. It is to be regretted in breech presentation. A distinction is not drawn between complicated and uncomplicated breech. The foetal mortality (3 stillbirths) in primigravid breech presentation (19 cases) is stated to be 15 per cent. What interests the obstetrician is the foetal mortality in uncomplicated primigravid breech delivery. This figure is obscure. But if we exclude 2 cases delivered by Caesarean section and 3 "associated with twins," then we have 3 stillbirths in 14 breech deliveries, i.e., 21 per cent.

Of 83 cases of persistent occipito-posterior position 29 were delivered by the forceps, 10 of these as unreduced posterior positions. Brow presentation deserves special mention. There were 8 (not 7 as stated) cases of brow presentation. All 8 were delivered by the vaginal route with 6 living infants (2 infants were stillborn, but in each case

the forceps had been applied unsuccessfully before the admission of the patient to hospital): there was no maternal death.

There were 4 cases of pubiotomy or symphysiotomy. Dr. Spain is convinced that these operations have a small but definite sphere of usefulness. He does not enlarge upon the indications for their use, but draws attention to the pelvic architecture of the subjects in which they were employed. In 3 the main feature was a narrow pelvic outlet. This indication is stressed by others who still find a limited place for these operations. In the 4th case there was narrowing of the mid cavity of an asymmetrical pelvis, due to inward bulging of an acetabulum. (Spelling in this section is rather eccentric.)

There were 17 cases of destructive operations on dead infants to facilitate delivery. These were mainly perforation of the foetal head. It is not made clear whether any difference is implied between "perforation of the head" and "craniotomy." There were 6 elderly primigravidae in this group and 4 of these had severe toxæmia. Caesarean section might have been preferable treatment. We are not told, however, which cases were "booked" and which were "emergencies" ("admitted at term in labour" might fall into either category.) It is difficult, therefore, to evaluate the line of treatment followed. There is no specific statement on the maternal result, save that 3 cases were morbid. While the presumption is that none died, the statement that 3 were morbid would be equally true if the 3 had died (B.M.A. standard).

There is a more liberal use of Caesarean section than formerly. There were 64 (not 63 as stated in the tables) cases of first Caesarean sections (including hysterectomies). It is stressed that all were lower segment sections. An arbitrary limit is not set to the number of repeat sections which can be carried out on the same individual provided they are lower segment operations, performed by

competent operators under good conditions. This view has allowed the more liberal use of the operation in the elderly primigravida, placenta praevia, toxæmia (for which 8 sections were performed), and certain other obstetrical conditions. There were 29 (not 30 as stated) "repeat" sections. There was 1 maternal death in the 93 cases. Except in a few cases of placenta praevia, the anaesthetic used for all sections was local infiltration with 0.5 per cent novocaine with, in addition, sufficient nitrous oxide and oxygen to allay the patient's anxiety. While there were no stillbirths, there were 8 neonatal deaths. In 5 of these the section was done for placenta praevia—in 3 (not 4 as stated) the child weighed less than 5 pounds. It is interesting to note that even though there were 5 neonatal deaths in the 20 cases of placenta praevia delivered by Caesarean section, in 10 cases of placenta praevia treated by Braxton-Hicks or internal version only 1 child survived.

The placenta was removed manually on 45 occasions. Most practising obstetricians would agree with the Master that, when haemorrhage is present, this is a simple and effective operation, provided it is done promptly while the patient's condition remains good. Doubtless the Master is equally right in his criticism that the blood transfusion situation in Dublin is unsatisfactory. In the only death in this series the removal was undertaken for retained placenta with postpartum haemorrhage. The patient did not have a blood transfusion. The cause of death was shock and haemorrhage.

The hospital morbidity on the B.M.A. standard is 1.78 per cent.

There were 17 maternal deaths. These are set out clearly in a table of some 6 pages. Four of these might be classed as 'avoidable'—1 case of puerperal sepsis in which many attempts at delivery before admission had failed; 1 of central placenta praevia when Caesarean section might

have been preferable to Braxton-Hicks version and the bringing down of a leg; 1 rupture of uterus which occurred (in a case undergoing trial of labour) while preparations were being made for Caesarean section; and the case of postpartum haemorrhage already referred to, when blood transfusion might have saved her.

Brief reports follow on external maternity cases, the infants', the gynaecological, the X-ray and the pathological departments.

This is not an easy report to read. The 17 pages of the summary are clear and interesting, but the tables of detailed cases make heavy reading. So much matter is contained under "remarks" that "summary of the case" would be a more accurate description. In spite of their being so long, information which would be of value is sometimes omitted, e.g., the degree of dilatation of the cervix when prolapse of the umbilical cord was first diagnosed. It seems undesirable to record in the tables under the heading "Result M.C." 'L' for a child which in fact died. An example of this is seen on page 45, Reg. No. 20850. Glancing quickly down the table it would seem that the result to all the children on that page was favourable. Only after reading a "remark", approximating to 40 words do we find out that the child whose "result" was said to be 'L' actually died. Why not record the result as 'N.D.' or 'Died' where it can be seen at a glance.

Even if somewhat heavy reading this is a most interesting report. Here we see reflected the outcome of vital thought. In this year's work we find the altering attitude to the elderly primigravida, placenta praevia, the severe toxæmia and Caesarean sections. That this is not mere change for the sake of fashion is to be gathered from Dr. Spain's remarks (page 16) on the subject of induction for suspect disproportion in the primigravida.

ANTHONY W. PURDIE.

Obituary

James Hendry

1886—1945.

THE death of James Hendry at the comparatively early age of 59 came as a grievous shock to his colleagues, and to his many friends and former pupils.

Hendry's qualities of character—simplicity, honesty of purpose, integrity and industry—were obvious; and you were not long in his company before his many-sided ability unfolded itself, and aroused ever-increasing appreciation and respect the more you got to know him. Not without these great qualities would his fellow undergraduates of Glasgow University have voted him into the Presidential Chair of the Students' Representative Council, and colleagues of later years have nominated him to serve on "The Interdepartmental Committee on Medical Schools" (Goodenough Committee). Such distinctions are not easily attained.

Reference to Hendry's undergraduate days would not be complete without a mention of his long services in and for the O.T.C. of Glasgow University. In the earlier months of the Great War of 1914-18 he was first captain and later adjutant of the Corps. In 1916 he went out to France and served as major with the R.A.M.C. until demobilization.

Hendry's entrance into the speciality of obstetrics and gynaecology was by an unusual route. He never did any spell of service as house physician or house surgeon in medical, surgical, or obstetric wards. He came direct to my department—introduced to me by my then senior assistant,

now Dame Louise McIlroy—from Professor Noel Paton's Physiological Laboratory, where he occupied the post of Muirhead Demonstrator. When I talked over the question of his transference to my department Noel Paton was laudatory as regards Hendry's ability; but he remarked that if I could get any writing out of Hendry it was more than he could ever accomplish. Curiously enough this particular dislike of writing persisted all through his professional life as my co-authors of the "Combined Textbook of Obstetrics and Gynaecology" can attest. By some, possibly by many, this may be accounted to him for righteousness in these days of literary verbosity and outpourings of pseudo-scientific "research." But in Hendry's case it was unfortunate because he, by reason of his extended scientific training in physiology and his post-graduate studies in the clinics of Germany and France—he spent close on 2 years abroad—had something to contribute that no other to a like degree possessed. Special mention should be made of the months he worked in the Clinique Tarnier, Paris, where he made contact with Professor Paul Bar whose investigations in antenatal physiology are even to-day recognized as of the highest quality.

Hendry's greatest literary contribution to our speciality—and it is of outstanding merit—are the chapters on the Physiology and Pathology of Pregnancy in "The Combined Textbook of Obstetrics and Gynaecology." When written for the first edition,



JAMES HENDRY

thought, and power of exposition he had few equals.

The President of our College, Eardley Holland, in the gracious tribute he paid to Hendry's memory in the columns of *The Times*, described him as "One of these rare people who with truth might be said to have no duplicate." Possibly he attempted too much—especially during the years of war—and thereby overtaxed his physical powers, great as they were. But this was inevitable! With Hendry the motive and driving power of all his activities were a high sense of duty and of service. Sir Hector Hetherington, Principal of Glasgow University, in a moving address at the memorial service held in the University Chapel on September 12th, refers to this in words which could not be more feelingly or gracefully expressed: "He had great natural gifts—tireless energy, a wide, exact and beautifully ordered memory, so that he could bring to bear on any situation the full range of his experience and knowledge, a cool and balanced judgment, executive skill of the highest order. And with these, kindness, patience, good humour, forthright honesty of purpose and of speech. But through it all there shone the deep devotion of a man to his duty."

We, his colleagues in obstetrics and gynaecology, mourn the loss of a great figure in our speciality. For what James Hendry accomplished, for his friendship, for his camaraderie, we place on record our heartfelt thanks. And in doing so we trust that this expression of our admiration may in some small measure bring comfort to Mrs. Hendry, as we feel sure it will be a source of pride and inspiration to their three sons.

JOHN MUNRO KERR.

his charm as a companion and his ability as an examiner would be incomplete.

I was privileged to be amongst his friends for over 20 years, a friendship which speedily grew into affection.

He was kind, generous and staunch. One could discuss anything with him with confidence and his advice on matters of practice, hospital problems, or University or personal affairs was always of value. He had a marvellous faculty of seeing the essentials of any subject and in discussion could put his points with a clarity which was the mark of a first class and at the same time practical brain.

It was a delight to travel with him on the Continent, which was my happy experience on numerous occasions as a fellow member of the Gynaecological Visiting Society. His organisation of our last two foreign journeys before the war—to Vienna and Budapest and Hamburg and Berlin—won for him the gratitude of the Society, while his fluent German gained our admiration and smoothed our way.

We were associated for 8 years as co-examiners in Glasgow and Belfast. In the past 25 years I have had many able and delightful colleagues but none to excel him. He was direct and practical; his questions clearly framed, varied and well expressed. Always courteous, the end of even the longest day found him alert, patient and good tempered. He had an unfailing instinct for the candidate with his goods in the window and speedily probed the depth of his knowledge.

Many happy memories are evoked by our evenings in both cities. Dining, either alone or with colleagues, he was a most agreeable and congenial host or companion. Blessed with a prodigious memory and a mine of general information, especially about his native Ayrshire and its links with Ulster, those evenings are the source of many a happy memory. In Belfast, as in

Any account of James Hendry which did not lay stress on his virtues as a friend,

Glasgow, his colleagues sincerely mourn his death.

The sympathy of all who knew him, and especially those who enjoyed the hospitality of his happy home will go out to Mrs. Hendry and to his three soldier sons, the second of whom is a member of our profession.

C. G. LOWRY.

It is hard to realise that James Hendry has really gone from among us and that he will no longer guide the destinies of obstetrics in Glasgow. To those closely associated with him he always gave the impression of tireless energy and enduring strength, which enabled him to accomplish successfully an amazing amount of work—a busy consulting practice, the exacting duties of teaching and administration associated with a University Chair, and invaluable service on hospital and national committees of one sort or another. In addition, he was always accessible to every student and young graduate, who sought advice or help. As his senior assistant for 9 years I know what a deep, personal interest he took in junior obstetricians, whether on his own staff or not. He encouraged us to attend and take part in

the various medical societies' meetings, at which he was a constant attendee; and we will remember those winter nights when he took us to the meetings of the Edinburgh Obstetrical Society, motoring home to Glasgow after midnight, when he was very much fresher than his juniors.

He was a very shrewd judge of character and this enabled him to choose his staff wisely. He greatly valued willing, loyal service and was most considerate of the feelings of all who worked under him down to the most junior nurse. As a result, he had the devotion of his ward sisters and nurses, whose main thought was the efficiency of the unit under an inspiring Chief.

His sound judgment, combined with an extraordinarily wide range of experience, made him an outstanding clinician and this was reflected in his brilliant teaching.

He was constantly thinking of the future, but unlike many planners, his plans were always workable and he knew how far it was practical to go. He had a driving force given to few men. He will be universally missed and by none more than his University in these days when someone with his qualities and experience is so sorely needed. I should like to record on behalf of all his assistants our particular sense of loss, since apart from gratitude for all he taught us, he was our constant counsellor and friend.

DUGALD BAIRD.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

A MEETING of the Council was held in the College House, on Saturday, 28th July, 1945, with the President, Mr. Eardley Holland, in the Chair.

Mr. Eardley Holland was re-elected President to take office in October next.

The following officers were also elected:

Vice-Presidents:

Professor D. Dougal.

Professor R. Marshall Allan.

Honorary Treasurer: Mr. W. Gilliatt.

Honorary Secretary: Mr. G. F. Gibberd.

Honorary Librarian: Mr. F. W. Roques.

Honorary Curator of Museum: Mr. A. W. Bourne.

The following candidates were elected to the Membership:

Trevor Montagu Barnett.

Alexander Buchan.

Daphne Wai Chan Chun.

Aileen Marian Dickins.

Ernest Dudley Yarnold Grasby.

Michael Willoughby Hemans.

Ursula Mary Lister.

Agnes Macfarlane Duncan Milne.

Abd-El-Salem Mahmood El-Minabbawy.

Kripananda Mitra.

Joan Pudsey Moignard.

Padma Raj.

Wallace Beresford Shute.

Beatrice Marian Smyth.

James Macbeth Thomson.

INDEX TO CURRENT LITERATURE

In this Index an endeavour will be made, so far as conditions permit, to maintain an up-to-date record of all titles bearing on obstetrics and gynaecology and the infant. The classification aims at making immediately available for the reader the titles under the various subject headings. In the majority of instances the title is obtained from the original publication. Where this has been impossible, the title has been obtained from the abstracting journal shown in brackets. Reprints will be welcomed and should be sent to the Editor.

Any inquiries should be addressed to Miss D. F. Atkins, British Post-graduate Medical School, Ducane Road, London, W.12.

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ANATOMY

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2. "Pelvic X-ray measurements and pelvic contraction." E. W. Frecker. *Med. Journ. Austr.*, May 26th, 1945, I, 532-7.
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NORMAL

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LACTATION

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The Relation of the Theca-Cells to Disturbances of the Menstrual Cycle

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INTRODUCTION.

IN a previous paper¹ it has been shown that when the theca-cells surrounding follicles of the baboon ovary proliferate or luteinize sufficiently extensively and are visible to the naked eye as yellowish plaques or masses, there is often an accompanying disturbance in the menstrual cycle in the form of bleeding, amenorrhoea, singly or in combination.

The literature contains numerous references to an analogous relation between thecal proliferations and menstrual irregularities in the human², but because these yellow masses of theca-cells are invariably related to atretic or cystic follicles, structures which by themselves are known to produce menstrual upsets, these theca-cells alone have been disregarded as significant in the production of such disturbances. The recent interest in the so-called rare tumours of the ovary, particularly the theca-cell tumours, has led to much speculation concerning the endocrine effects of the various components of the normal ovary. Originally oestrogen was believed to arise only from granulosa-cells. Then Zondek suggested that the theca-cells elaborated greater quantities of oestrogen than

did granulosa-cells³ and when it was shown that theca-cell tumours exerted profound oestrogenic influences⁴ it was generally accepted that theca-cells were capable of hormone-secretion. The precise character of the hormone elaborated by these cells is still debated. Although some clarification has been made there is still disagreement as to its precise nature. Some of the obstacles to a proper appreciation of the hormonal effects of the theca-cells are no doubt due to the irreconcilable viewpoints concerning the origin, action and potentialities not only of the theca-cells but also of the other constituents of the ovary, namely the granulosa- and stroma-cells. The clinical effects of theca-cell tumours or proliferations of these cells cannot be satisfactorily appreciated without recognition of the functional capabilities of each of the ovarian components.

The effect of luteinization in theca-cells is still conjectural. There is as yet no conclusive evidence by which luteinization in theca-cell tumours can be regarded as exerting different functional effects than the non-luteinized or partially luteinized variety.

Although theca-cell proliferations with luteinization have been frequently observed

and recorded in relation to the lutein cysts of chorionepithelioma and hydatidiform mole, corpus-luteum cysts, theca-lutein cysts, follicular cysts and persistent corpora lutea, correlation with coexistent uterine reactions has not been properly established. Whatever the uterine disturbances occurring simultaneously with any of these pathological states within the ovary, whether irregular cycles, haemorrhage or amenorrhoea, it was the follicle that was generally conceded to be at fault. It did not seem to matter whether the follicle contained granulosa-cells, whether the granulosa-cells were degenerating or multiplying, or whether they were luteinized. Nor did the size and the number of cysts, the extent of any alterations in their intrinsic or surrounding structure seem to influence the generally accepted notion that the follicle, *per se*, was responsible for the co-existing uterine disturbances. Why the luteinized theca-cells, the occurrence of which is common to all of these pathological states, should have been almost completely disregarded except by a few observers is reasonably apparent. Firstly, the alterations in the theca-cells of the human ovary are less obvious or are of seemingly less significance than those in the follicles to which they are usually related. Secondly, despite the clinical finding of sterility, haemorrhage or amenorrhoea, endometrial biopsy, which is a commonly adopted procedure in the diagnosis of menstrual vagaries, occasionally does not accurately reflect ovarian dysfunction when such in fact exists.

Because in the baboon ovarian dysfunction could be estimated by fluctuations of the sexual skin apart from menstrual disturbances⁵ and because ovarian and endometrial biopsies could be obtained repeatedly if necessary at specific times in the cycle, a relation was shown to exist between extensive theca-luteinization and irregularities of the menstrual cycle. Since

the essential characteristics of the ovario-uterine relation of the human and the baboon are very similar, it appeared likely that an analogous syndrome existed in the human.

In this communication, the characteristic alteration of theca-cells in the human ovary which lead to the formation of yellow plaques will be examined. The various stages in the life cycle of these reactions will be shown and a classification based upon their morphological characteristics is suggested. Evidence will be presented to show that luteinization of such theca-cells is a frequent finding in abnormal menstrual rhythm and is probably causally related to the uterine aberrations which may be encountered. Finally, an analysis of these findings will be made in an attempt to correlate these thecal reactions with the known functional aberrations of other thecal structures, namely, the theca-cell tumours.

MATERIAL.

The material which forms the basis of this study was collected during the past 8 years. The ovaries and uteri were obtained from women who had been operated upon because of excessive bleeding or other uterine evidence of endocrine disorder. Many of these patients, in the 4th and 5th decades of life, had experienced a satisfactory childbearing career. Owing to the supervention of irregular cycles and profuse bleeding they were constrained to seek medical advice. When both ovaries had been removed at operation they were cut serially and the sections stained with haemotoxylin and eosin. Sharlach R was used for occasional sections from each ovary and clear sections used for refraction study with the polarizing microscope.

OBSERVATIONS.

The extent of ovarian participation in the cycle of the human female is not so great as that which occurs in lower forms.

The number of human primordial follicles maturing in each cycle is much less than in ovaries of other primates. Whereas in the baboon as many as 60 follicles may mature, in the human not more than 8 or 10 ripening follicles are encountered in each cycle,⁶ and whereas corpora lutea are produced in abundance in many mammals it is rare in the human, as in the baboon, for more than 1 to be produced at a time.

Since the rhythmical uterine changes in the human are much more pronounced than those in other mammals, the physiological stimuli arising out of follicular growth, corpus luteum formation and regression of these processes must be relatively more intense in the human than in other species. In other words, the achievements of many follicles by way of uterine growth, in say the baboon, is accomplished by a single follicle in the human. Any pathological variation in the cyclical activity of human endometrium must therefore be induced by relatively less apparent dysfunction in the ovary than would occur in other mammals. Realization of this fundamental characteristic of the human ovary is essential for an appreciation of how slight may be the aberration necessary to interfere with the normal rhythmic changes in the endometrium.

In normal ovaries the incidence of theca lutein cells apart from those related to corpora lutea is not easily established since the ovaries, as a rule, are removed for some gynaecological complaint. Luteinized theca-cells in ovaries obtained in this way occurred more frequently in our series than was originally anticipated, and their extent and distribution was not always reflected clinically by the severity of the menstrual disorder. Mild irregular bleeding was associated with extensive theca-cell luteinization and conversely, profuse haemorrhage occurred with only slight thecal activity. In general, the pattern of thecal proliferation

in the human was the same as that which was encountered in the baboon.

The theca of ripening follicles. Around the primordial follicle, the theca is barely if at all distinguishable from the surrounding stroma. With ripening of the follicle some alteration may begin to occur, although this is not a constant feature. The cells of the theca interna may differentiate and become distinct from the theca externa while cells of the latter retain their similarity to surrounding stroma. The cells comprising the many layered theca interna may show intense activity despite the small size of the ripening follicle to which they *may be related*. They are usually closely packed, but may be separated by oedema; they are large, round or polyhedral, often with indistinct outlines. The cytoplasm is finely granular, pale and may contain lipid particles. The latter are more in evidence in later stages when regression of the follicle commences or has been in progress for some time. The nuclei are ovoid or round, single or binucleate and usually eccentrically situated. Mitotic figures may be numerous (Fig. 1). Sometimes theca-cells retain these epitheloid characteristics long after follicular atresia has commenced. In addition they may luteinize and persist when evidence of the follicle to which they were related has disappeared. Shaw⁷ states that proliferation and hypertrophy of theca-interna-cells continue in the atretic process and that the cells become scattered among the neighbouring stroma-cells. That they may be evident in the stroma surrounding corpora albicantia is confirmed by our own observations. Luteinization of theca-cells is independent of granulosa-cell luteinization since it may occur not only when the granulosa-cells do not luteinize but also in the complete absence of the latter. Since these alterations in theca and granulosa may occur only in isolated areas

of a follicle they may not be observed except in serial studies.

The process of follicle ripening is not invariably accompanied by differentiation of the theca. A large number of follicles ripen, attain maximal size, regress and disappear without any visible alteration of the surrounding theca-cells. Why some maturing follicles should not show any visible thecal differentiation whereas others have an extremely active and well differentiated theca has not been determined.

The theca of atretic follicles. Theca-cells are most constantly observed at the periphery of corpora lutea. At this somewhat advanced stage of their life cycle they, like the granulosa-cells, are also luteinized and form the para-lutein-cells of the corpus luteum. The characteristics of the luteinization observed in these cells are but rarely seen around cystic or atretic follicles. When theca-cells around cystic follicles do present the typical features of para-lutein-cells there is frequently also some luteinization of the granulosa-cells. This type of cyst is observed in the presence of chorionepitheliomata and hydatidiform moles, and is known as a theca-lutein, paralutein or lutein cyst. Such a cyst may be indistinguishable from cysts of the corpus luteum. Cysts of the corpus luteum are usually recognized by their large central cavity, the central coagulum, the presence of a lutein layer of granulosa-cells, and by the clinical evidence of prolonged progestational activity. These criteria for cysts of the corpus luteum are not sufficiently adequate to differentiate such structures from a follicle which has failed to rupture and in which luteinization of theca and granulosa particularly has occurred. It is therefore possible that many structures considered to be cysts of the corpus luteum are theca-lutein cysts in which luteinization of granulosa is extensive although not as great as that occurring in the theca-cells.

Active proliferation and luteinization of theca-cells may occur, as has been indicated, without luteinization of the granulosa. Fig. 2 shows part of the wall of a follicle in which luteinization of the theca is marked. There were numerous mitotic figures among the theca-lutein-cells (Fig. 2) indicative of pronounced theca-cell activity. The intense capillary permeation and intercellular haemorrhage exceeded normal intensity. The granulosa-cells were also increased in number and contained many mitotic figures but did not show characteristic features of luteinization as normally encountered in corpora lutea. Such a structure may be devoid of granulosa-cells in which case it may be regarded as a theca-lutein or paralutein cyst. Between the two extremes one, where the granulosa occurs throughout the cavity and the other, where no such cells are found, wide variations in the ratio between theca- and granulosa-cells may be encountered. In either of the granulosa or theca layers luteinization may occur in all or part of the cells present.

Luteinization of theca-cells around atretic follicles has been observed in ovaries with a co-existing corpus luteum and is of regular occurrence in early pregnancy. The process may also be extensive in the presence of persistent corpora lutea. Such a relation during the menstrual cycle is, however, rather infrequent and of limited extent. The involvement of large numbers of theca-cells, visible macroscopically as yellow plaques, henceforth termed corpora thecale lutea, was not observed in conjunction with corpora lutea in this series.

In addition to the finding of varying proportions in the numbers and degree of luteinized cells, differences in the character of the luteinization may also be observed. In Fig. 3 the thecal reaction is less frequently encountered than those so far described, but it illustrates a variation in the lutein change which may occasionally be ob-

served. These cells surround an atretic follicle in which the granulosa-cells have completely disappeared and into which there has been extensive haemorrhage. The large number of vessels with thick muscular walls permeating the theca form a useful criterion for the identification of the thecal nature of this structure since such vessels never permeate granulosa-cells. In corpora lutea they extend between lobules of granulosa-cells but not among the cells themselves. An intense vascular response with capillary haemorrhage into the interstices of theca-cells is a familiar and frequently associated finding in diffuse theca luteinization. A high power study of this section (Fig. 3a) reveals the lutein-like nature of the reaction. This is not apparent in studies with low magnification, and is therefore unlike corpora lutea in this respect. High magnification reveals a large clump of cells which are strikingly similar to the luteinized theca-cells shown in Fig. 2. In some specimens the relation is only demonstrable in studies with oil-immersion. It is this type of lutein reaction, limited in extent in this specimen, which we have encountered in the yellow plaques at the periphery of atretic follicles. The ovary from which this section was obtained contained several such areas of theca-cells unrelated to each other.

Figs. 4 and 4a illustrate cytoplasmic changes in theca-cells around an old atretic follicle, identical with those which occur in corpora lutea. Here, however, the nuclei have retained their original stromal features and, in many instances, have undergone little change. The demarcation between cell forms is not abrupt.

The lutein theca-cells so far described occur around follicles in which the general form of the follicle is retained. The lining of such a follicle may be that of endothelium or degenerating and flattened, not easily identifiable, granulosa-cells. The

atretic follicle is usually regarded as having a layer of centrifugally proliferating theca-cells separated from the cavity lining by a layer of hyaline. The atretic follicle may not always be apparent despite thecal proliferation and luteinization. The fluid from its cavity is absorbed or perhaps is replaced by connective tissue and hyaline deposition (Figs. 5 and 5a). In such instances one finds a solid mass of theca-cells without a central cavity and the peripheral part of the mass is continuous with the surrounding parenchyma. There is no evidence of encapsulation, and medium-sized blood vessels pass from unaltered theca through the luteinized theca-cells without interruption. Although the cells of the corpus thecale luteum merge with the cells of the stroma there is frequently a distinct demarcation between the two. The corpus thecale luteum may contain undifferentiated theca-cells identical with those of the surrounding stroma.

The most frequently observed response in theca-cells within the ovaries from women with manifestations of gynaecological endocrine disorders is represented in Figs. 5a and 6a as well as in Fig. 7a. These cells do not resemble the lutein-cells previously described. They contain a more finely granular cytoplasm. The nuclei are neither as large nor as pale. Frequently the similarity is so slight that any relation between the 2 types appears remote. However, when these theca-cells are compared with the para-lutein-cells of an approximately 30-day-old corpus luteum there is no doubt as to their similarity. Figs. 7 and 9 show such corpora lutea and the detailed structure of their theca-cells. When the latter are compared with those of the corpora thecale lutea in Figs. 5a, 6a, 7a (high power sections of Figs. 5, 6 and 7 respectively), the pale, finely granular cytoplasm and deeply stained nuclei are readily discernible. The fat content of such cells is

high and is represented in 'haematoxylin and eosin stained sections by clear spaces. Their similarity to the cells of the adrenal cortex is remarkable and is probably not without significance. The gross appearance of masses of these cells is that of pale or deep yellow plaques variable in size, some no larger than a pin head. There may be one or several in number and they may be scattered throughout the ovary. The point at which they may be regarded as theca-lutein-cell tumours is debatable. Since these masses of theca-cells are able to revert to their stromal form whereas theca-cell tumour growth appears to be an irreversible process, this feature of reversibility, on the one hand, and irreversibility, on the other, would seem at present to be a distinguishing characteristic between the 2 conditions. From the foregoing it is apparent that theca-cell proliferations with or without luteinization may occur with any of the recognized forms of follicular degenerations.

Because of their relation to various types of atresia, the following classification for theca-cell proliferations is suggested on the basis of a nomenclature applied to the Graafian follicle by Aschoff.

I. *Corpus thecae luteum.*

- (a) Without granulosa-cells or with degenerating granulosa-cells. (These give rise to para-lutein or theca-lutein cysts).
- (b) With luteinized granulosa-cells. (These produce lutein cysts usually associated with chorionepithelioma and may be confused with persistent corpora lutea).

II. *Corpus thecae luteum fibrosum.*

III. *Corpus thecae luteum candicans.*

IV. *Corpus thecae luteum hyalinum.*

V. *Corpus thecae luteum restiforme.*

In Group I the original form of the follicle is retained, the granulosa-cells may be degenerating; the theca may, in part, retain stromal features and hyaline deposition may have occurred between the theca and basement layer of granulosa cells or their remains. (Luteinization of granulosa-cells in cystic or atretic follicles without any coincident change in theca-cells gives rise to a granulosa lutein cyst. Though probably related to the structures enumerated above, it is not considered in this classification of thecal reactions.)

In Group II granulosa cells are not present, absorption of liquor folliculi has taken place, the cavity is filled with a few connective tissue cells and a hyaline ring may be found around these cells. External to this ring are found the luteinized theca-cells.

Group III represents lutein reactions occurring around a collapsed corpus atreticum in which the hyaline laminae of opposite sides, when they exist, become opposed with obliteration of the central cavity.

In Group IV there is a lutein reaction surrounding follicles in which collapse has not occurred, but hyaline tissue invades the cavity with a few nucleated connective tissue cells.

Group V indicates a lutein reaction around primordial or small maturing follicles. These were not observed, but are theoretically possible.

It must be appreciated that in proliferation and luteinization of theca interna during follicle degeneration, the extent of the thecal process is variable. It may be very slight or it may permeate extensively in an eccentric or centripetal manner through the stroma and so give rise to the various patterns which are observed in these states. Furthermore, the classification does not take into consideration quantitative values of activity which may be of paramount significance in attempting to assess the

endocrine effects of these reactions upon the uterus.

It has thus been shown that the theca-cells surrounding a maturing follicle may behave in one of several ways. They may not undergo any change whatsoever regardless of whether the follicle attains full size before becoming atretic. Sometimes intercellular oedema and pervasion of the theca interna by blood capillaries and lymphatics are the only visible alterations which have occurred before atresia commences. Variations of the atretic process may have their beginnings in the first part of the cycle for that is when the atretic process is first evident even in normal cycles. When the normal sequence of events which usually result in ovulation and corpus luteum formation is disturbed, atresia and corpus thecale luteum formation is one of the expressions of such dysrhythmia which eventually leads to menstrual anomalies. The alteration in the character of the theca-cells whereby they assume epitheloid features, acquire fat and take on the peculiarities of lutein-cells and lay down hyaline tissues, may have its physiological culmination in the formation of yellow masses, the cells of which resemble paralutein-cells approximately 30 days old. The alterations in the theca may proceed and its fat content increase. Finally they may revert to their original or stromal character with complete loss of thecal identity.

The follicle around which thecal activity is observed may be atretic and collapsed, there may be extensive haemorrhage into or around its cavity, its granulosa-cells may be completely or partially destroyed and the latter may be luteinized to greater or lesser degree. The theca-cells may extend into the stroma of the ovary in an eccentric fashion and may form a mass of considerable size comparable in extent to that of a corpus luteum. Such a structure is here termed a corpus thecale luteum.

The frequency with which these formations of theca cells are encountered in association with some menstrual anomaly suggests that the disturbances in menstruation are occurring as a result of the corpus thecale luteum. However, the theca-cells, like the uterine aberration, may be merely an expression of the same endocrine dysfunction. Causal relation may not exist.

Although the endometrial pattern in the presence of theca-cell luteinization does not concern us at this stage it may not be amiss to indicate some of the observations which were made in this respect. The diversity in the pattern of theca-cell reactions may be associated with corresponding varieties of endometrium but a lack of material forestalls at present any statistical analysis of such a relation. A wide range in the uterine reactions and clinical disturbances is nevertheless observed in the material so far studied. Fig. 10 illustrates the endometrium which occurred with the theca-cells represented in Figs. 6 and 6a. According to the classification they are of type I(a).

This patient, Mrs. T., age 50, had prolonged bleeding with excessive menstrual loss and irregular cycles for 2 years preceding operation. The duration of menses was usually 2-3 weeks during this time. The endometrium showed cystic dilatation of some of the glands of the same specimen.

Mrs. H. A., age 48. (Microphotographs are not represented since the thecal reactions were not strikingly different from those of the previous case.) This patient supposedly reached the menopause at the age of 40, 8 years prior to admission. Three months previously she commenced bleeding and continued with moderately heavy loss until operation.

The uterus contained a thick polypoid endometrium and there was luteinization of the theca interna around several follicles. Intense haemorrhage was noted around several follicles in the same ovary, but this may have been due to operative trauma.

Fig. 11 is from endometrium observed in a case to which the thecal reaction, the most

extensive yet encountered, was of Type III. In this endometrium there is complete inhibition of gland formation in all layers, only the superficial epithelium retaining any semblance of normalcy. The reaction here is suggestive of androgenic inhibition.

Mrs. V., age 34, para 2, from whom this endometrium was obtained, had bled excessively with each period over the past 2 years. Her menses usually lasted 2-3 weeks. Previous cycles had been normal. Four transfusions, each of 500 c.cm. of blood, were required prior to operation.

Occasionally normal endometria were observed despite the presence of luteinized theca-cells and abnormal menstrual symptoms. In one of the patients under observation, the theca-cell reaction was of Type III (Fig. 7). The endometrium in this instance was very thick, soft and spongy, like that of an early pregnancy. The history was as follows:

Mrs. K., age 36, para 2, was admitted because of irregular menses, menorrhagia and metrorrhagia. Menses originally occurring at 28 day intervals now varied between 25 and 30 days. Frequently they were accompanied by flooding and clots and persisted for 7-8 days. A curettage was performed on first admission and bleeding subsided during her stay in hospital but, at the next cycle, brisk uterine haemorrhage ensued and operation was then performed.

Mrs. H., age 34, para 3, youngest aged 5. Fig. 3 (Type I(a)). She had no abnormal or irregular bleeding, but there was profuse pre-menstrual discharge and low mid-line abdominal pain during the week preceding the onset of bleeding. These symptoms were of 2 years duration.

The utilization of a classification for these thecal proliferations may eventually yield more information on utero-ovarian relation. So far, however, the limited available material has not afforded any reasonable correlation between the menstrual disturbances, the endometrial pattern and the extent or nature of the peri-follicular reactions, except that such exist.

DISCUSSION.

(a) Terminology.

The origin of lutein theca-cells from the theca interna of atretic follicles was first recognized by Limon in 1903⁸. These cells had previously been observed in the ovaries of cats and dogs by Pflugger, but their precise nature was conjectural until the present century. Schroen in 1863, regarded them as fragments of disintegrating corpus luteum, Schulin⁹ described them as epithelial structures and Harz in 1883 believed that they were offshoots of glomeruli of the kidney. The formations of theca-cells vary in different species so that it is difficult to draw conclusions as to their function in the human based upon observations in other species. The term 'interstitial cell' was applied by the earlier workers to the cells which were derived from the theca interna. Separation of these cells from the theca externa in the ovary of the rabbit leads to the formation of gland-like masses and to these masses in this animal was first applied the term 'interstitial gland'.¹⁰ On morphological evidence alone an endocrine action was attributed to the interstitial cells by the workers prior to the discovery and isolation of the ovarian hormones. It had been recognized that in some species these cells increased at the time of sexual maturity and then diminished with age. Furthermore, a reciprocal relation with the corpus luteum was also apparent, since the interstitial glands of some species decreased with the first appearance of the corpus luteum.¹¹

With the passing decades and the advent of the recent knowledge regarding hormones, less attention was directed to the histological study of these interesting cells. Shaw's histological studies in 1925⁶ provided a fertile oasis of slowly accumulating knowledge concerning the 'nature and action of these cells in the human. Recently, there has been a renewed interest in their

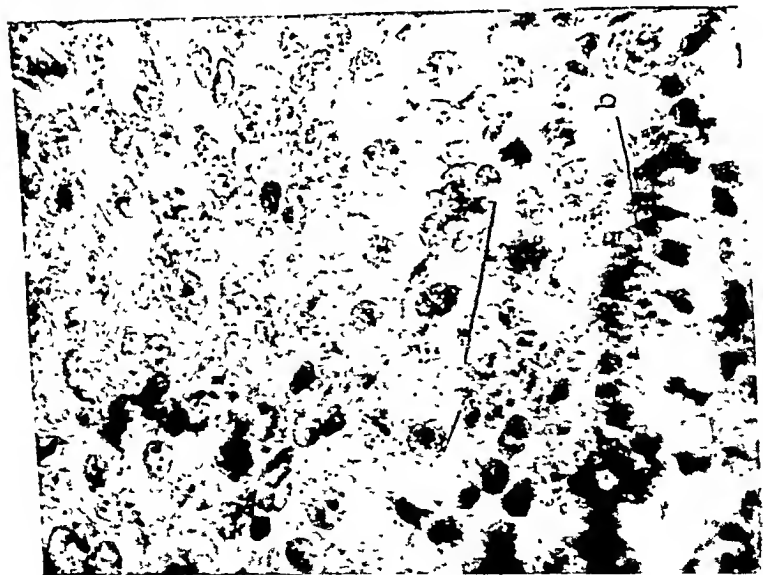


FIG. 1.

- (a) Theca interna of a normal ripening follicle showing enlargement of the nuclei and occasional mitotic figures.
- (b) Granulosa-cells lining wall of the follicle.

A.C.

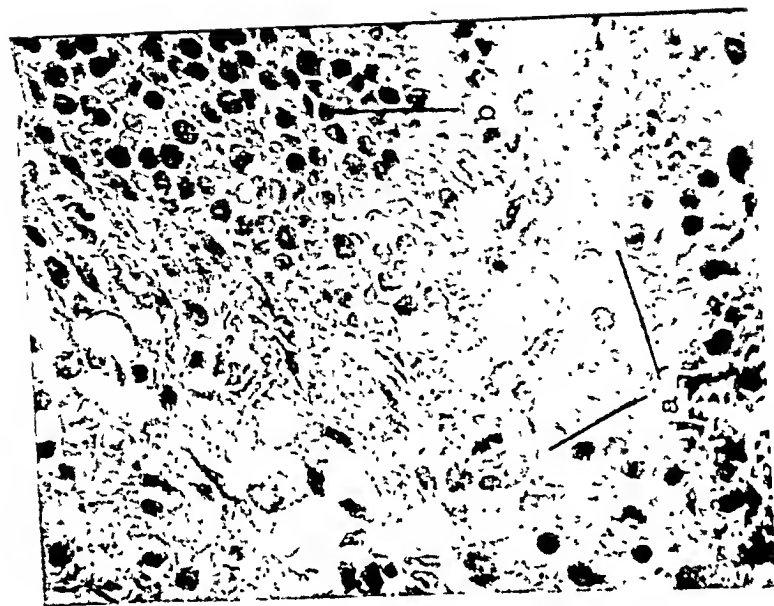


FIG. 2.

- (a) Luteinized theca-cells. Note mitosis.
- (b) Granulosa-cells without luteinization and with mitosis.



FIG. 3 ($\times 80$).
follicle devoid of a haemorrhagic

- (a) Theca cells.
(b) Cavity of follicle filled with blood and few connective tissue fibres

A.C.

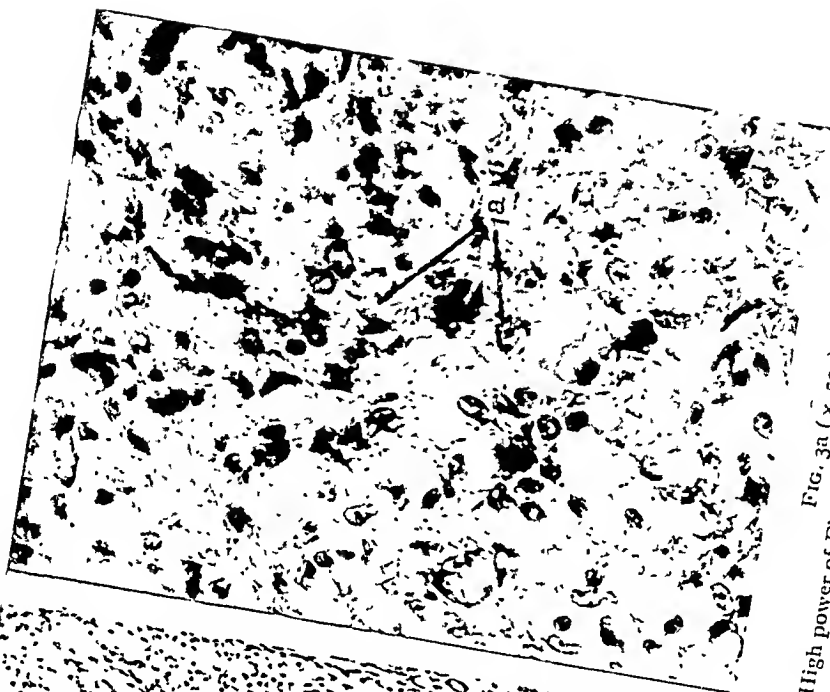


FIG. 3a ($\times 520$).
High power of Fig. 3 showing clumps of theca lutein cells (a).

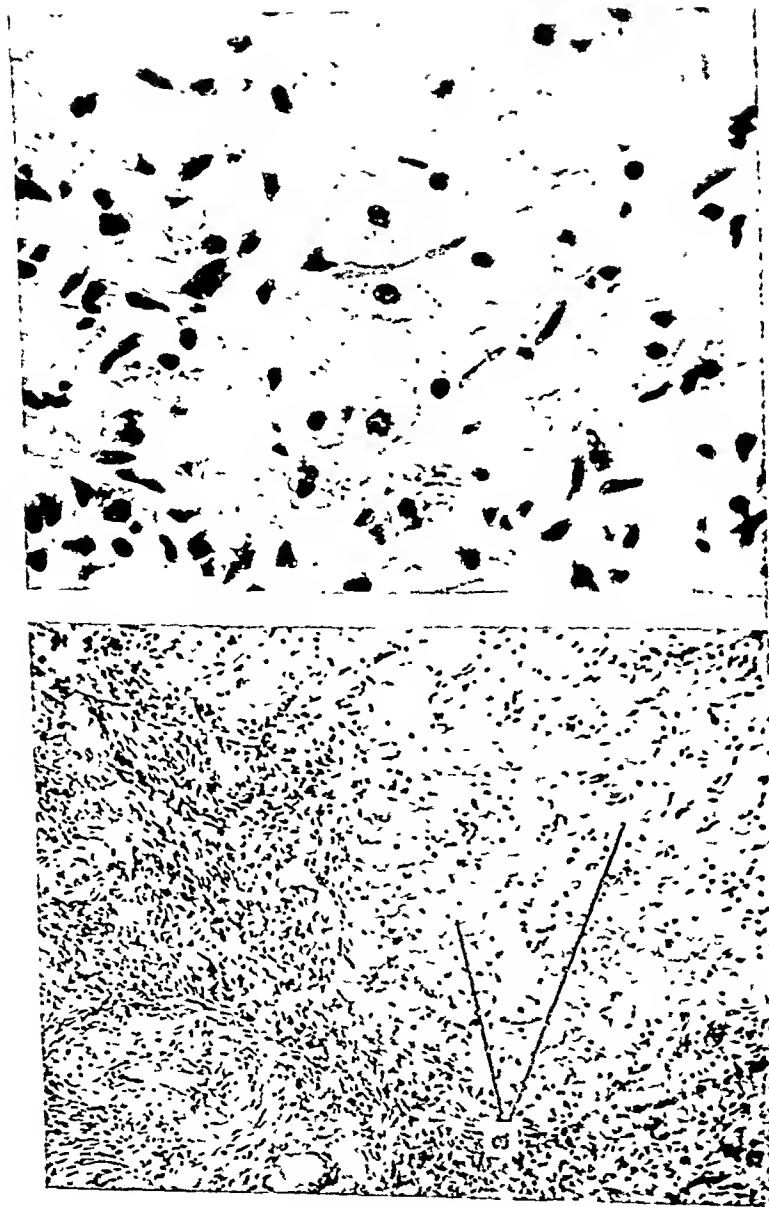


FIG. 1 ($\times 50$).

(a) Showing theca-cells with cytoplasmic changes characteristic of luteinization but without very marked nuclear alterations. Phagocytic brown staining cells were very numerous in the cavity of this follicle.

FIG. 2 ($\times 520$)
High power of Fig. 1.

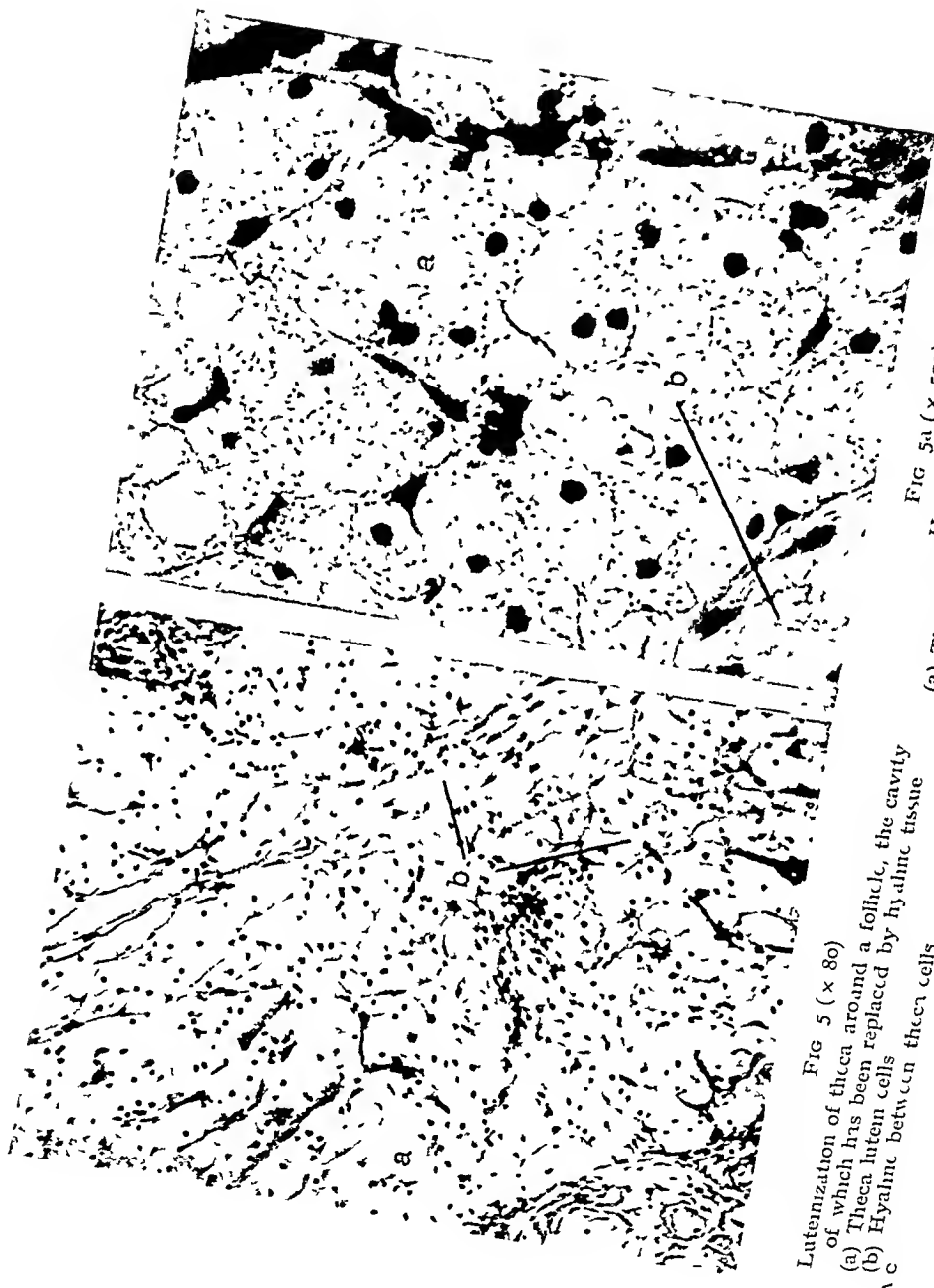


Fig 5 (x 80)
of which has been replaced by hyaline tissue

- (a) Theca lutein cells
- (b) Hyaline between theca cells

Fig 5a (x 520)
High power of Fig 5

- (a) The typical granular changes of luteinization in the cytoplasm of theca cells
- (b) Hyaline between theca cells

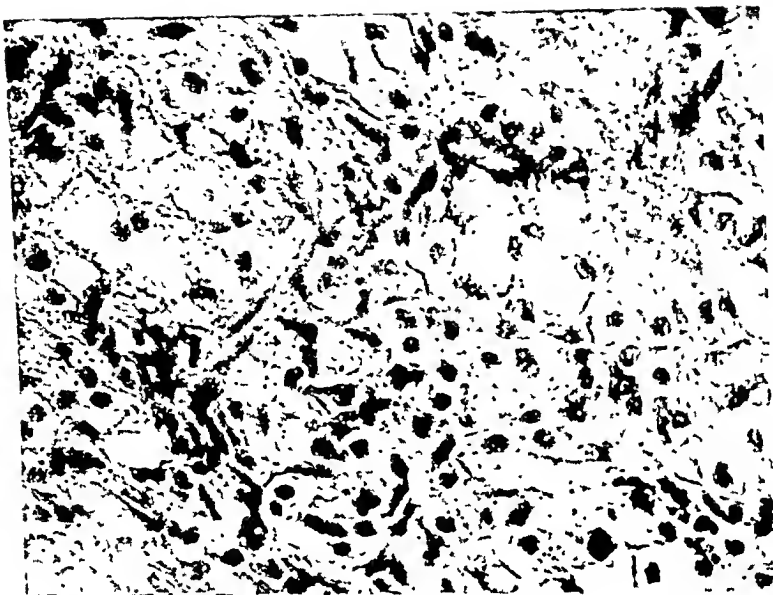


FIG. 6a ($\times 520$).
High power of theca cells in Fig. 6.



FIG. 6 ($\times 80$).
Thecal luteinization around an atretic follicle.
(a) Lutein theca-cells.
(b) Cavity of follicle.

A.C.



FIG. 7 ($\times 80$).
Lutein theca-cells without any evidence of a follicle
The admixture of undifferentiated and lutein theca-
cells is evident in this specimen.

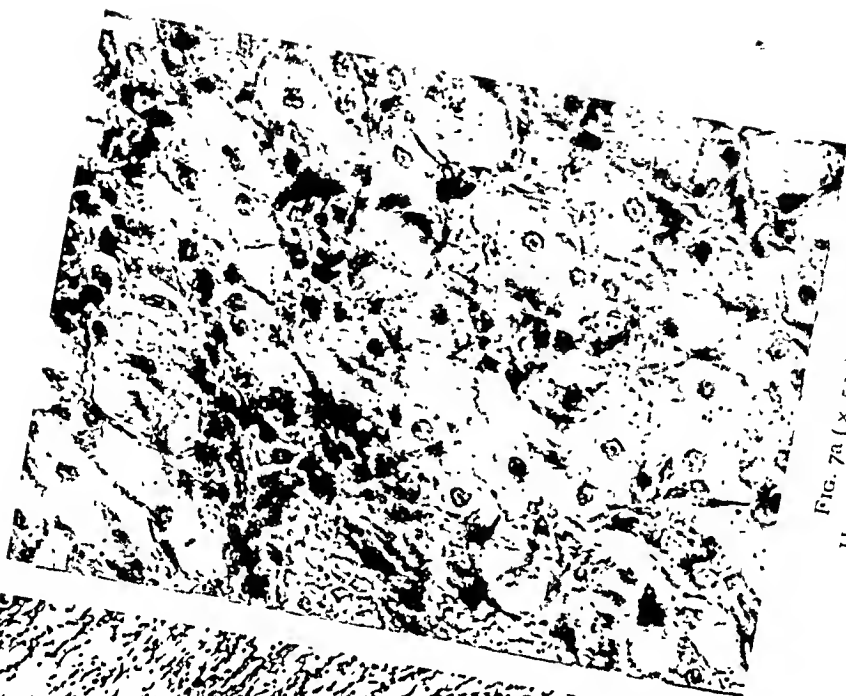


FIG. 7a ($\times 530$).
High power of FIG. 7.

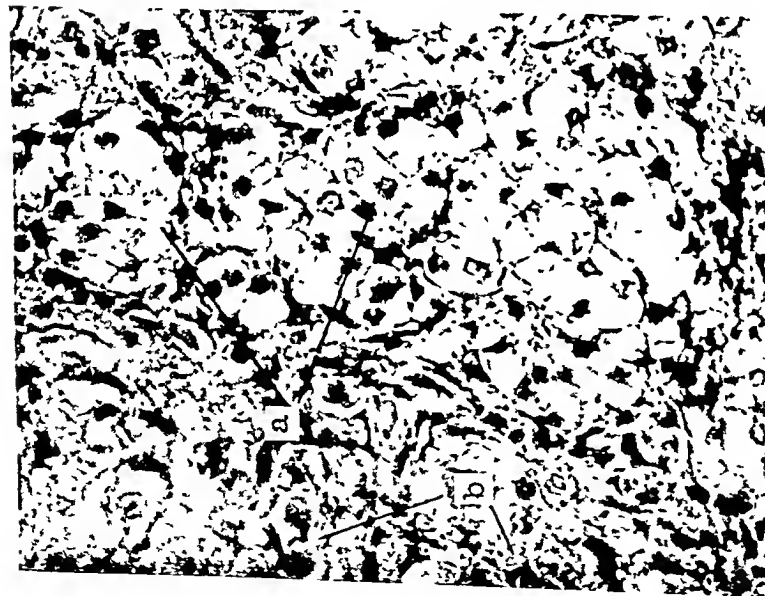


FIG. 8
Corpus luteum, approximately 30 days old
(a) Paralutein-cells (compare with Fig. 6a)
(b) Granulosa-cells

A.C.

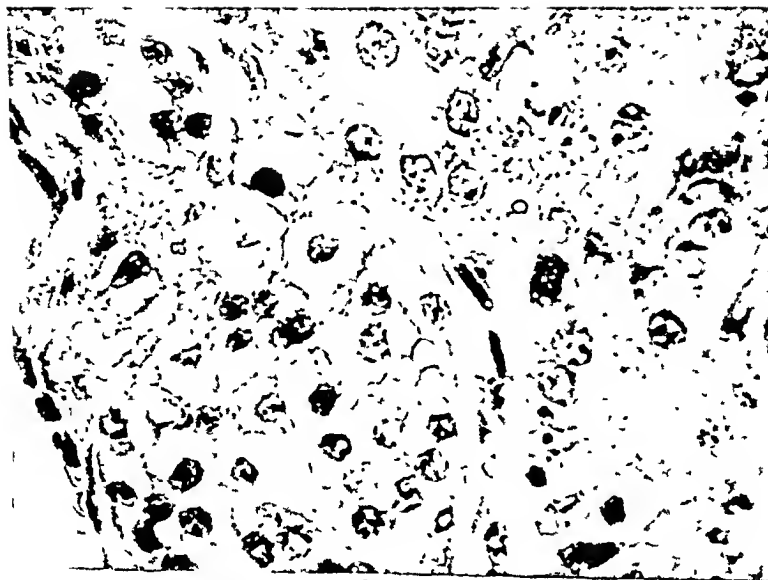


FIG. 6.
Corpus luteum, approximately 16 days
(a) Paralutein cells.
(b) Granulosa-cells



Fig. 11.

Endometrium (Case Mrs. V.) with complete inhibition of gland formation.
(a) Superficial epithelium of uterine cavity.



Fig. 10.

Endometrium from same case as Figs. 6 and 6a, showing cystic dilatation and normal progesterational glands.

function in view of the potential relation of the cells to the theca-cell tumours. Shaw's work and the studies of his predecessors indicated that in the human the theca lutein cells remained confined by the external theca of the follicle, and the cells rarely were scattered through the ovary. Hence, the interstitial gland was not a usual constituent of the human ovary, apart from aggregation of thecal cells confined to the follicle. The occurrence of these cells was indicative of follicular atresia. This author, from his morphological evidence revived the plausible suggestion of a theca-cell endocrine function. Since then the controversy of whether these cells have a hormonal action, or are merely a manifestation of a degenerative process, continues to exist. It has been shown, though not conclusively, that they contain oestrogen, but whether they act as storage depots or actually produce the hormone is also conjectural. With the introduction of endocrine concepts, the problem of the function of these cells and the structures they form has assumed additional complexity.

The word 'lutein' was originally applied to a cell which had a yellow appearance due to the presence of a pigmented fat, the nature of which was at that time unknown. By common usage, the term has been applied to the corpus luteum, both granulosa- and theca-cells. Recently, advantage has been taken of the knowledge that the lutein cells of the corpus luteum form progesterone, to label as true luteinization only those tissues which function as a source of measurable amounts of progesterone. This extension of the meaning of 'lutein' is, in our opinion, unjustified, and in this discussion further attributes than are implied in the original use of the term will now be considered. Any cell within the ovary, whether granulosa or theca, which, because of the pigmented fat it contains, produces a yellow colour macroscopically,

will be considered as a lutein cell, paralu-
tein referring specifically to the theca-cells of a corpus luteum. One other item of descriptive terminology is of some concern. Many terms have come into use in connexion with theca-cell proliferation and luteinization. The variations in these terms are so great that the precise meaning intended by the respective authors has been lost. May the term 'interstitial gland', which was first applied to normal gland-like thecal reactions in the cat, be applied with justification to thecal reactions in the human, where they normally do not form a gland-like structure, nor do they function as a physiological unit in the cyclical phenomena of the ovary? Furthermore, it has been shown that in rodents, the interstitial gland is not derived solely from theca interna but that it is derived partly from germinal epithelium.¹² The term 'interstitial gland', therefore, seems inappropriate for the human and only further studies upon the comparative physiology of these cells can unfold the obscurities of the problem. Consequently, the use of the terms, interstitial cells, interstitial gland, interstitial mass and interstitial body will be discontinued in this discussion where it refers to human theca-cell reactions. On the other hand, the retention of the term theca tends to correlate the benign reactions of these cells with the activity encountered in thecomas and lutein theca-cell tumours to which they are undoubtedly related. Despite the rejection of terminology which is applied to thecal reactions in lower forms their similarities are not disregarded. There seems little doubt that the thecal proliferations in human and other forms arise as a direct or indirect result of pituitary (ICSH) stimulation.¹³ The fact that they occur in the human as a regular event, not only during the early part of pregnancy when placental gonadotrophes exist in large quantities, but also during the normal or aberrant menstrual

cycle, supports the contention that a pituitary factor is responsible for these changes.

(b) *Developmental Considerations.*

The theoretical determination of the endocrine function of any group of cells sometimes entails embryological considerations. Much of the controversy regarding the endocrinal function of theca-cells revolves, unimportant as it may be, around the question of whether these cells, derived from mesenchyme, can produce the same hormone as the granulosa-cells which are derived, according to some, from coelomic epithelium. Because they are morphologically the same as the interstitial cells of Leydig in the testis, it has been suggested that they are the site of ovarian androgens,^{14, 15} again an assumption based upon embryological data, subsequently supported by experimental evidence. Much of the confusion regarding the hormonal rôle of these cells is based upon the present unsatisfactory knowledge concerning the development of these cells. Because there is still conflicting information regarding the nature of the secretions produced by the individual components of the ovary and concerning the capacity of these elements to alter the character of the particular hormones they produce, many of the hypotheses in regard to the origin of these hormones have been based upon embryological assumptions, themselves not in complete accord.

Elaboration upon this aspect of thecal activity is not the purpose of this paper, but one consideration regarding the embryological theca-granulosa relation is of some significance in understanding the reactions of theca-cells in the adult ovary. The most recent work¹⁶ concerning the embryology of the human ovary disclaims a unified origin of theca- and granulosa-cells, and attributes the origin of granulosa-cells to

coelomic epithelium. The dependence of the oogonium, which has an independent origin to that of either theca- or granulosa-cells, upon the symbiotic and correlated activities of these latter structures throughout their life cycles is established. The fate of the ovum is shown to be dependent upon the synergistic action of theca- and granulosa-cells. This synergism is maintained throughout the life of these cells. It is, therefore, not surprising that the multiple variety of thecal reactions observed in the adult are invariably related to the function of the follicle. The histological similarity between theca-cells and granulosa-cells in their many activities within the ovary such as occurs in corpora lutea, in corpus luteum cysts and in lutein cysts and corpora aberrantia¹⁷ is a time-honoured one in the life cycle of these cells, for in the primitive ovary the granulosa-cells which encircle the oogonium are at one stage indistinguishable from the theca-cell primordium which surrounds them.

The fate of these structures seems to be determinedly interwoven from the time of their inception in the foetal ovary to the senescent phase of their existence. It is logical that all cell-structures within the ovary act harmoniously and function as a correlated mechanism. Alteration in the function of the follicles may conceivably alter the reactions in the theca, although destruction of the former does not necessarily prevent further proliferation of luteinization of the theca.¹⁸ Because of this mutual affinity, the cells of the theca interna are capable of reacting in the manner which has already been described, that is, by proliferation and hypertrophy with resulting epitheloid features. When atresia occurs, these cells may luteinize before reverting to their original form, a faculty of which granulosa cells are incapable. Since the theca is not specific for any given follicle and may become related to a new follicle

merely by displacement and rotation of the follicle during the ordinary course of maturation, such a theca retains its capacity to proliferate in a new sphere of follicular influence. Therefore, the theca of a given follicle may have been related, or come to be related, to any other follicle within the same ovary and it has a capacity for differentiation, proliferation and dedifferentiation greater than that of any other tissue within the ovary.

(c) *Formation of Corpora Thecae Lutea.*

In the aberrant processes of thecal proliferation which are observed long after any evidence of the originally related follicle, it is apparent that the extent of thecal change in many instances, exceeds the limit of what is commonly regarded as theca interna. Since theca interna and theca externa both arise from mesenchyme it is conceivable that the latter may respond in given circumstances to the same stimuli as does the theca interna. It would seem that the specific reactions which are commonly observed in theca interna occur because of a spatial relation to the granulosa-cells or the ovum of the follicle. Furthermore, that under the conditions which lead to the formation of corpora thecae lutea, where extensive areas of the ovary have been involved, the development potentialities of the theca externa have been evoked, and consequently it is capable of luteinization in the same way as does the theca interna. The theca, therefore, not only maintains its capacity to proliferate, but it is capable of calling upon its reserve in the surrounding parenchyma when the occasion demands.

The dynamic character of theca-cells is indicated not only by their capacity for change, but also by the presence of mitoses even in their lutein form. Mitoses in granulosa-lutein-cells, on the other hand, have not occurred in our experience. Once a

corpus luteum is produced, the granulosa-cells form a very stable structure with little, if any, capacity for continued growth. That lutein changes may occur in the theca of a follicle before ovulation has occurred with remnants of the ovum *in situ*, suggests" that aberration of the menstrual cycle, in so far as it may be due to thecal activity, may have its beginnings in the first part of the cycle. The second part of the cycle, dominated by the corpus luteum, may reasonably be expected to be less subject to disturbances than the first part when atresia is first apparent. The contention has been made²⁰ and investigations in this laboratory support this view, namely, that disturbances in the menstrual rhythm are essentially the result of aberrations in the follicular or first phase of the cycle, and that the corpus luteum phase is the most precise in the duration and the stability of its activity.

The various forms of thecal reactions which have previously been classified, obviously have different potentialities according to the ratio of luteinized and non-luteinized theca and granulosa-cells. The precise nature of their specific activities is not yet fully apparent in view of the limited extent of available material upon which such a study must be based. Certain characteristics have, however, become obvious as has already been shown.

(d) *Clinical Considerations.*

In the presence of the corpus luteum of menstruation, the proliferation of theca cells is not invariably as great as that which occurs in its absence. A similar relation as previously noted, has been observed in other species where the normally occurring interstitial body begins to disappear when the corpus luteum first forms. Some of the normal progestational endometria which were observed in conjunction with microscopical thecal proliferations may have been

due to the influence of a co-existing corpus luteum. In one case under observation the endometrium (of ovary, Fig. 7) simulated an early pregnancy reaction, but without villi, and was extremely hyperplastic. Goodall²¹ refers to a uterus which possessed all the characteristics of a 3 months pregnancy, except that neither a pregnancy nor a corpus luteum was present in either ovary. One ovary contained follicular cysts, the largest of which had "a thin sickle of internal capsule lutein-cells covering the circumference of the sclerosed cyst wall." The phenomena of bleeding and amenorrhoea in luteinization of the ovary may perhaps further be illustrated by reference firstly, to a patient observed by Dougal²² with a history of 9 months' irregular haemorrhage followed by 5½ months' amenorrhoea, preceding operation for a primary chorionepithelioma of an ovary. The uninvolved ovary, 4 times normal size, contained numerous cysts which microscopically were composed of lutein tissue, and scattered about the ovary were numerous islands of lutein cells; secondly, to a study by Robinson²³ of several patients, ranging in age from 15-32, in whom luteinization of theca interna occurred. In 3 cases the complaint was menorrhagia, in 1 sterility and irregular cycles, and in 2, amenorrhoea of 4 and 12 months' duration respectively. All, according to the author, were cured by resection of that part of the ovary containing the luteinized patches. The luteinization of theca-cells may, like a corpus luteum, inhabit follicle rupture,^{24, 25} so that resection of these cells, while not directed at the prime agent of the disturbance may, like other more empirical methods, restore normal cycles as occurred in these particular instances. In comparing our own series with that of Robinson, the similarity in the symptomatology is obvious, despite the fact that the age groups are dissimilar. Sterility was not a feature of

the older group, some having had as many as 7 children, in an adequate reproductive life. It is quite possible that the ability of theca-cells to luteinize, produce uterine upsets and revert to its stromal form, may be sufficient to produce a temporary sterility as observed in some instances. In the words of Goodall, "One is apt to assume that any disease that has overstepped the bounds of normal restraint and of normal demarcation must then, *ipso facto*, run the whole gamut of pathological destruction. Nothing could be further from the truth."

The endocrine nature of the theca-cells has been discussed elsewhere,¹ but there are several clinical phenomena, the explanation of which has been difficult, and which in the light of what has been said concerning these cells may have a tentative solution.

The greatest incidence of menstrual irregularities and haemorrhage occurs at puberty and at the menopause. It is generally assumed that these irregularities are due to a failure of the follicular processes to lead to ovulation. The endometria in many of these cases show at least some progestational response. Such endometria are certainly compatible with theca lutein proliferations around atretic follicles in the absence of corpora lutea. One need only consider the influence of small doses of thyroid in many sterilities to appreciate how delicate is the endocrine balance necessary for the maintenance of proper function.

(e) Relation to Tumours.

The virilizing effect of certain lipoid-cell tumours of the ovary, theca-cell tumours and lutein thecomas, is not without its counterpart in the follicular theca-cell proliferations.^{26, 27} These latter reactions are prominent at the *menarche*¹¹ and menopause.²⁸ There is increased androgen excretion not only during the progestational phase of the cycle²⁹ but there is a rise, tem-

porary in nature, during the menopause.³⁰ According to Hamblen there may also be a reduction in the androgen output following oöphorectomy in young women. These androgen variations, relative to ovarian function, and the hirsutes of the menopause may indicate the virilizing effects of theca-cells during the periods of ovarian activity when they are in evidence. Shaw suggests that secondary sex characteristics are determined by theca-cells.

Not only are the similarities between the corpora thecale lutea and theca-cell tumours clinical in their nature, but they are most in evidence in histological examinations. Firstly, when the tumours undergo luteinization they do so in the same manner as the Graafian follicle³¹; they may be composed of large epithelioid fat containing cells similar to those described around atretic follicles, and they are invariably characterized as being separated by masses of hyalinized connective tissue plaques.³² This latter feature which is often emphasized as characteristic of the tumours is merely an exaggeration of a process which is of common occurrence in normal ovaries. The "glass membrane" described in all the older textbooks is nothing more than hyaline deposition which occurs during normal follicular atresia.

The oestrogenic manifestations which sometimes occur in theca-cell tumours are associated with the presence of doubly refractile fat and, according to Geist,³² when the fat is scant oestrogenic manifestations are absent. The visible fat in theca-cell tumours is, in part, a cholesterol or cholesterol ester and is limited almost entirely to the cellular elements comprising the tumour. In the connective tissue it is found only in tiny scattered globules. The distribution of fat in corpora thecale lutea is of a similar nature. As to its character, our observations reveal that it is doubly refractile and therefore of the type which,

according to Geist, exerts an endocrine actions.

It is thus apparent that the histological features of the cellular components of some theca-cell tumours are in no way radically different from the exaggerated theca-cell proliferations observed in follicle atresia. The clinical characteristics of the tumour formations may be merely the exaggeration of the reactions which apparently occur with the modified and limited theca-cell reactions around atretic follicles and therefore they do not differ radically in this respect from the tumours of other endocrine glands.

SUMMARY AND CONCLUSIONS.

1. Theca-cell proliferation may occur as part of the maturation process in the Graafian follicle.
2. Theca-cell luteinization around atretic follicles may be without clinical significance in ovulatory cycles, but are nevertheless a part of the normal atretic process.
3. Luteinized theca-cells exert an endocrine influence, the precise nature of which is as yet undetermined.
4. The formation of extensive areas of lutein theca-cells may be visible macroscopically and appear as pale yellow masses or plaques usually associated with atretic or cystic follicles which, however, may not be readily apparent.
5. Luteinization of theca-cells may be localized to small areas and, consequently, serial sections of ovaries may be necessary to determine the presence of luteinized theca-cells.
6. In the presence of extensive thecal luteinization associated with follicular atresia, disturbances of menstrual rhythm and bleeding may ensue.
7. The term "corpus thecale luteum" has been suggested for the thecal proliferations occurring in association with follicular

atresia, and a classification for the types of these reactions has been proposed.

8. The character of the uterine reactions associated with theca-cells is such that neither oestrogenic nor progestogenic influences can be attributed to them. Their activity suggests the formation of a third ovarian hormone which may exert androgenic activity, or of a modified secretion of the known varieties which is capable of distorting the balance between simultaneously acting steroid hormones of the menstrual cycle.

9. The relation of these structures to theca-cell tumours has been briefly reviewed.

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Blood-pressure of Relatives of Patients with Toxaemia of
Late Pregnancy
(A Preliminary Note)

BY

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A RISE of blood-pressure is one of the cardinal signs of the toxaemias of late pregnancy. The object of this study is to attempt to assess what part, if any, hereditary factors play in the causation of the hypertension.

HEREDITY IN HYPERTENSIVE DISEASE.

It is well known that high blood-pressure and the diseases associated with it, such as angina pectoris, coronary thrombosis and cerebral haemorrhage may affect several members of the same family. It is regrettable that reliable statistical study of the familial incidence of high blood-pressure or its mode of inheritance, if any, is not to be found in the literature, though many records of individual families in whom several members, often in 3 or 4 generations, have been affected, are available. Additional evidence on this point has come from the studies of Hines and Brown.¹ Using the "cold pressor test" they were able to demonstrate that 75 per cent of hyper-reactors gave a family history of hypertension and that the reaction to the cold pressor test follows an inherited pattern, though not every individual with a hyper-

reaction necessarily develops hypertension. It is doubtful, however, whether a high reaction to the cold pressor test is of any value in predicting the occurrence of toxaemia of pregnancy. Browne,² in a study of this test, found that a peak of 150 mm. of mercury or over in early pregnancy was a fairly good, but not invariable, indication that a patient would develop toxaemia. A high basal level was a more reliable indication. Reid and Teel³ found the test of no value in predicting toxaemia. Thus, even if the reaction to the cold pressor test follows an hereditary pattern, this is not necessarily related to the occurrence of pregnancy toxaemia.

The present state of our knowledge of heredity in hypertensive vascular disease was summed up by Maurice Campbell⁴: "There is an obvious need for much more knowledge as regards the inheritance of arteriosclerosis, especially along 2 lines—accurate statistics as to how common such positive histories are; and detailed genealogical trees in some large families with precise notes about general build, blood-pressure, etc., and causes of death. Until these data are available our conclusions must be general ones; that a tendency to

arteriosclerosis is frequently inherited, that it sometimes affects particular organs producing several cases of, say, cerebral haemorrhage in one family, and that there is some slight evidence that the underlying diathesis is inherited as a dominant Mendelian character." These words were written in 1933, but as yet reliable statistical evidence along the lines suggested has not appeared.

HEREDITY IN ECLAMPSIA.

A good many reports have appeared of the occurrence of eclampsia in several members of the same family. A tendency to hypertensive disease in relatives of patients suffering from eclampsia and toxæmia of pregnancy has also been noted.

Theobald⁵ described a family in which both parents died of Bright's disease. Five of their children died of cerebral haemorrhage, 1 of angina pectoris, 1 of tuberculosis, 1 surviving has a very high blood-pressure and 1 died of eclampsia, though there was some doubt in the last case regarding the nature of the disease, since the patient survived 1 month, and Theobald stated that she probably died from uræmia. In the next generation 1 grandchild died of cerebral haemorrhage, 1 of eclampsia, 1 of tuberculosis and 3 surviving had high blood-pressure. The same author⁶ also found a family history of hypertension in 6, possibly 7, out of 9 patients admitted to hospital with high, or rising blood-pressure in pregnancy.

Bickenbach and Kroning⁷ found that 4 out of 39 eclamptic patients had 1, 2, or more cases of eclampsia in the same family. They calculated that this is a much greater familial incidence than could be expected if it were due to chance alone.

Reports of the occurrence of eclampsia, toxæmia and hypertensive disease in members of the same family have come from

many other authors including Dieckmann,⁸ Malpas,⁹ Nevermann,¹⁰ Tillmann and Herrick,¹¹ Eastman,¹² and Plass.¹³

On the other hand, great caution must be observed in cases in which hypertensive disease occurs in relatives of patients with eclampsia and toxæmia of pregnancy. The reason for this is that hypertensive disease is so very common. Robinson and Brucer¹⁴ showed that over 40 per cent of the adult population of the United States of America are actually or potentially hypertensive, and there is no evidence to show that this finding cannot be equally well applied to the inhabitants of Great Britain. Apart from the numerous well authenticated cases of the occurrence of hypertensive disease in several members of the same family, there is no reliable statistical evidence regarding the hereditary factors concerned; this evidence, which could only be derived from a prolonged statistical survey, is urgently needed. It is clear that if hypertension affects over 40 per cent of the adult population, the chances are considerable that several members of the same family may suffer from the disease without there necessarily being any hereditary element. It will be shown in the present study that severe hypertension was found in relatives of pregnant patients who were treated as controls and who were not suffering from toxæmia.

CLINICAL MATERIAL.

This investigation has been carried out since 1938 in the Obstetric Unit at University College Hospital. The object of the study was to determine what part, if any, a familial tendency to hypertension plays in the aetiology of pregnancy toxæmia. The blood-pressure was estimated in 226 blood-relatives of 129 patients who had been admitted to hospital with pregnancy toxæmia. The blood-pressure was also

estimated in 66 relatives of 47 patients who were not suffering from toxæmia but had been admitted towards the end of pregnancy for some other reason, such as antepartum hæmorrhage. The estimations of blood-pressure were made when the relatives came to the hospital to visit the patients. In any case in which the blood-pressure seemed abnormally high it was retaken after a period of rest.

Several difficulties have been encountered in carrying out this investigation. Patients admitted to the hospital are drawn from a wide area in Greater London and beyond, and it is often difficult for their relatives to get to the hospital to visit them. This has been aggravated by war conditions which have led to scattering of families and transport difficulties. Insufficient records are available to allow of statistical analysis of the results, and in the majority of cases the family record is incomplete, so that pedigrees cannot be constructed to show the incidence of high blood-pressure. It is hoped to carry on the work at University College Hospital and it is also to be hoped that other workers, in districts where some of the difficulties that have been found in dealing with London patients and their relatives are not so pressing, will be stimulated to carry out research along similar lines.

CLASSIFICATION OF CASES OF PREGNANCY TOXAEMIA.

The cases of pregnancy toxæmia in this series have been divided into groups to correspond with the classification which is in use in the Obstetric Unit at University College Hospital. A brief *résumé* of this classification will be given and further details can be found in "Antenatal and Postnatal Care" by one of us (F.J.B.).¹⁵ Two modifications have been made for the purposes of this paper. Cases of eclampsia

are considered in a separate group and cases of chronic nephritis and pregnancy have been excluded since there were insufficient numbers of cases in this group. In addition, a case of acute yellow atrophy of the liver is not available.

Toxæmias of late pregnancy are classified as follows:

1. Pre-eclamptic toxæmia and eclampsia.
2. Chronic glomerular nephritis and pregnancy (nephritic toxæmia).
3. Essential hypertension in pregnancy.
4. Acute yellow atrophy of the liver.

A patient is said to be suffering from pre-eclamptic toxæmia if a rise of blood-pressure above the normal level of 120/80 occurs after the 20th week of pregnancy. In nephritic toxæmia, pregnancy has supervened in a patient already suffering from chronic nephritis. In essential hypertension and pregnancy the blood-pressure has been found to be above the normal level of 120/80 before conception or in the first 20 weeks of pregnancy. Cases in which an abnormally high blood-pressure is recorded after the 20th week of pregnancy and in previous records of blood-pressure are not available cannot be placed in any of the groups in this classification and thus are called cases of "unclassifiable toxæmia."

The blood-pressures of relatives of patients suffering from toxæmia are classified in the 4 groups: eclampsia, pre-eclamptic toxæmia, essential hypertension and pregnancy, and unclassifiable toxæmia. These are given in Tables I to IV. Blood-pressures of relatives of patients in the control group who did not have toxæmia are given in Table V.

It must be noted that the majority of the records in cases of toxæmia refer to patients with toxæmia severe enough to warrant admission to hospital. Patients are admitted for toxæmia if the blood-pressure reaches 150/100; if there is a rise of blood-

TABLE I.

Blood-pressure of Relatives of Patients with Eclampsia.

| No. | Father | | | Mother | | | Brothers | | | Sisters | | | Remarks |
|-------|--------|----------------|-----|--------|----------------|----|----------|----------------|----|---------|----------------|----|---------|
| | Age | Blood-pressure | | Age | Blood-pressure | | Age | Blood-pressure | | Age | Blood-pressure | | |
| | | S. | D. | | S. | D. | | S. | D. | | S. | D. | |
| F 191 | — | 170 | 100 | 51 | 110 | 70 | | | | 20 | 114 | 68 | |
| F 531 | 48 | 128 | 60 | 48 | 130 | 70 | | | | 18 | 142 | 76 | |
| G 36 | — | — | — | | | | | | | — | 110 | 78 | |
| H 89 | 68 | 160 | 100 | 60 | 160 | 76 | | | | 30 | 136 | 74 | |
| L 173 | — | — | — | 61 | 154 | 90 | | | | — | 108 | 82 | |

TABLE II.

Blood-pressure of Relatives of Patients with Pre-eclamptic Toxaemia.

| No. | Father | | | Mother | | | Brother | | | Sisters | | | Remarks |
|---------|--------|-------------------------|-----|--------|-------------------------|-----|---------|-------------------------|----|---------|-------------------------|----|-------------------------|
| | Age | Blood-pressure S. D. | | Age | Blood-pressure S. D. | | Age | Blood-pressure S. D. | | Age | Blood-pressure S. D. | | |
| 651/34 | | | | 72 | 164 | 74 | | | | | | | |
| 779/29 | | | | 68 | 186 | 110 | | | | 40 | 110 | 70 | |
| 249/34 | | | | | | | | | | 40 | 100 | 56 | Recurrent toxaemia |
| 1022/33 | | | | 55 | 170 | 90 | | | | | | | |
| A 775 | | | | 68 | 248 | 110 | | | | | | | |
| D 726 | | | | 54 | 146 | 84 | | | | 32 | 128 | 70 | |
| B 565 | 60 | 120 | 70 | 61 | 120 | 90 | | | | 28 | 100 | 60 | Recurrent toxaemia |
| B1329 | | | | | | | | | | — | 124 | 80 | |
| A1287 | | | | 62 | 130 | 74 | | | | | | | Recurrent toxaemia |
| D 778 | | | | | | | | | | 20 | 136 | 72 | |
| D 935 | | | | | | | | | | — | 120 | 80 | |
| E 534 | | | | | | | — | 196 | 80 | 42 | 160 | 78 | |
| | | | | | | | | | | 32 | 136 | 62 | |
| E 377 | | | | 56 | 140 | 76 | | | | — | 104 | 56 | Twins |
| E 381 | | | | | | | | | | 35 | 136 | 74 | Twins |
| | | | | | | | | | | 32 | 128 | 74 | |
| E 27 | | | | 66 | 200 | 110 | | | | 36 | 150 | 70 | Twins. Sister is a twin |
| E 442 | | | | | | | | | | 45 | 150 | 84 | |
| E 596 | | | | | | | | | | 38 | 146 | 88 | |
| E 436 | | | | 56 | 144 | 66 | | | | | | | Niece 18, 150/80 |
| E 830 | 44 | 150 | 100 | 43 | 220 | 120 | | | | | | | 1st preg. normal |
| E 770 | | | | 64 | 150 | 80 | 31 | 154 | 72 | 26 | 138 | 76 | 2nd preg. toxaemic |
| E1002 | | | | 64 | 216 | 100 | | | | | | | Recurrent toxaemia |
| F 243 | | | | 45 | 134 | 80 | | | | | | | |
| F 375 | | | | | | | | | | 29 | 124 | 64 | |
| F 388 | 61 | 174 | 95 | 57 | 175 | 120 | | | | 24 | 110 | 75 | |
| | | | | | | | | | | 23 | 120 | 65 | |
| G 6 | | | | 46 | 110 | 78 | | | | 19 | 120 | 78 | |
| G 1. | | | | | | | | | | 25 | 108 | 80 | |
| Z 75 | | | | | | | | | | 34 | 120 | 68 | |

TABLE II (Continued).

| No. | Father | | | Mother | | | Brother | | | Sisters | | | Remarks |
|-------|--------|-------------------------|-----|--------|-------------------------|-----|---------|-------------------------|----|---------|-------------------------|----|--|
| | Age | Blood-pressure S. D. | | Age | Blood-pressure S. D. | | Age | Blood-pressure S. D. | | Age | Blood-pressure S. D. | | |
| G 72 | | | | 56 | 154 | 90 | | | | | | | Twins |
| G 575 | | | | 52 | 138 | 78 | | | | | | | |
| G 471 | | | | 64 | 160 | 110 | | | | 31 | 138 | 80 | |
| G 148 | | | | 67 | 184 | 92 | | | | 18 | 128 | 78 | |
| G 592 | | | | 56 | 138 | 80 | | | | | | | |
| G 634 | | | | 56 | 138 | 68 | 19 | 128 | 60 | | | | |
| H 28 | | | | 56 | 142 | 76 | | | | | | | |
| H 91 | | | | | | | | | | 40 | 136 | 74 | |
| H 391 | | | | 64 | 150 | 98 | | | | | | | |
| E 554 | | | | | | | 46 | 168 | 92 | | | | |
| H 373 | | | | 59 | 146 | 70 | | | | | | | Aunt, 52, 150/80 |
| H 484 | | | | 48 | 158 | 70 | | | | 26 | 122 | 78 | |
| H 620 | | | | | | | | | | 28 | 80 | 50 | |
| H 782 | | | | — | 132 | 60 | | | | | | | |
| J 8 | | | | 53 | 134 | 70 | | | | | | | |
| H 852 | | | | 57 | 120 | 80 | | | | | | | |
| H 812 | | | | 53 | 180 | 110 | | | | | | | |
| H 826 | | | | 46 | 140 | 80 | | | | | | | |
| H 833 | | | | 60 | 130 | 90 | | | | | | | |
| J 13 | | | | 68 | 138 | 85 | | | | | | | |
| J 46 | | | | 49 | 140 | 80 | | | | | | | Father died of stroke Recurrent toxæmia |
| J 235 | | | | | | | | | | 25 | 130 | 80 | |
| J 245 | 56 | 156 | 80 | 56 | 212 | 120 | 28 | 130 | 80 | | | | |
| J 299 | 67 | 138 | 78 | 69 | 170 | 100 | 29 | 126 | 76 | | | | |
| C 466 | | | | 72 | 190 | 112 | | | | 40 | 120 | 76 | |
| | | | | | | | | | | 37 | 120 | 78 | |
| J 623 | | | | 61 | 160 | 105 | | | | | | | |
| J 676 | | | | 45 | 185 | 110 | | | | 23 | 135 | 75 | |
| E 293 | | | | | | | | | | — | 120 | 85 | |
| K 6 | 60 | 130 | 70 | 50 | 166 | 90 | | | | 26 | 122 | 70 | |
| K 51 | | | | — | 120 | 80 | | | | 26 | 122 | 70 | Aunt 64, 160/82 |
| K 85 | | | | 64 | 180 | 90 | | | | | | | |
| K 538 | | | | | | | | | | 35 | 154 | 88 | |
| K 547 | 55 | 186 | 110 | 63 | 146 | 84 | | | | 17 | 128 | 80 | |
| K 580 | | | | 49 | 176 | 100 | | | | 13 | 100 | 40 | |
| K 586 | | | | 58 | 140 | 92 | | | | 38 | 130 | 76 | |
| | | | | | | | | | | 22 | 126 | 78 | |
| | | | | | | | | | | 19 | 120 | 80 | |
| K 604 | | | | 67 | 220 | 130 | | | | | | | |
| K 662 | | | | — | 150 | 100 | | | | | | | |
| K 978 | | | | | | | 33 | 100 | 55 | 37 | 120 | 65 | Aunt 64, 160/82 |
| L 261 | | | | | | | | | | 38 | 148 | 92 | |
| | | | | | | | | | | 31 | 150 | 70 | |
| L 333 | | | | | | | | | | 35 | 110 | 60 | |
| L 432 | | | | 59 | 150 | 86 | | | | | | | |

TABLE III.

Blood-pressure in Relatives of Patients with Essential Hypertension in Pregnancy.

| No. | Father | | | Mother | | | Brothers | | | Sisters | | | Remarks |
|-------|--------|-------------------------|-----|--------|-------------------------|-----|----------|-------------------------|-----|---------|-------------------------|-----|---|
| | Age | Blood-pressure S. D. | | Age | Blood-pressure S. D. | | Age | Blood-pressure S. D. | | Age | Blood-pressure S. D. | | |
| Ar359 | | | | | | | | | | 44 | 118 | 70 | Mother died of congestive heart failure, and asthma |
| C 426 | | | | | | | | | | 39 | 138 | 98 | |
| C 540 | | | | 63 | 154 | 64 | | | | 27 | 124 | 70 | |
| E 487 | | | | 51 | 186 | 90 | 28 | 150 | 90 | 36 | 96 | 60 | Mother's sister, 51 B.P. 196/126. |
| E 499 | | | | 51 | 136 | 76 | | | | 32 | 138 | 84 | |
| E 873 | | | | | | | | | | 23 | 156 | 76 | |
| F 281 | | | | 62 | 230 | 110 | | | | 38 | 132 | 96 | |
| F 302 | 51 | 162 | 62 | 50 | 224 | 116 | | | | 31 | 154 | 90 | |
| F 392 | — | 146 | 72 | | | | | | | 30 | 132 | 64 | |
| F 435 | | | | 50 | 148 | 80 | | | | | | | |
| F 447 | | | | 61 | 180 | 90 | | | | | | | |
| G 308 | | | | 58 | 192 | 112 | | | | | | | |
| G 583 | | | | | | | | | | 44 | 190 | 116 | |
| | | | | 65 | 196 | 100 | 41 | 138 | 72 | 42 | 176 | 84 | |
| H 43 | | | | | | | | | | 34 | 180 | 84 | |
| H 77 | | | | 74 | 200 | 84 | 49 | 140 | 72 | 24 | 122 | 64 | |
| H 152 | | | | | | | 42 | 128 | 68 | 44 | 160 | 80 | |
| | | | | 57 | 210 | 100 | | | | 35 | 124 | 76 | |
| C 540 | | | | | | | 24 | 140 | 100 | 33 | 150 | 80 | |
| J 652 | — | 165 | 100 | | | | | | | 29 | 130 | 72 | |
| J 927 | | | | 58 | 230 | 110 | | | | 36 | 96 | 60 | |
| K 157 | | | | — | 152 | 100 | | | | | | | Father's sister, 176/100 |
| K 225 | | | | 45 | 160 | 90 | 17 | 120 | 70 | 14 | 108 | 60 | Mother's sister, 188/72 |
| | | | | 58 | 180 | 96 | | | | — | 190 | 90 | |
| L 6 | | | | | | | | | | | | | Father has heart disease |
| L 159 | | | | | | | | | | 58 | 158 | 110 | Mother died of stroke |
| | | | | 59 | 158 | 100 | 31 | 118 | 76 | 34 | 112 | 72 | |
| L 230 | 54 | 146 | 90 | | | | | | | 22 | 100 | 76 | |
| L 466 | | | | 48 | 160 | 100 | — | 128 | 78 | | | | |
| L 503 | | | | 64 | 150 | 90 | 29 | 110 | 70 | 30 | 120 | 70 | |

pressure with albuminuria; or if there is oedema. Patients with mild toxæmia which does not reach these standards are treated as out-patients.

RESULTS OF THE INVESTIGATION.

Table I gives the blood-pressure in 12 relatives of 5 patients who suffered from eclampsia—admittedly a very small num-

ber. While the fathers of 2 of the patients and the mother of 1 were definitely hypertensive, the blood-pressure in the relatives of the remaining patients was within normal limits. This shows that eclampsia does occur in patients who have no familial predisposition to hypertensive disease.

Table II gives the blood-pressures in 106 relatives of 70 patients with pre-eclamptic toxæmia. Forty-nine of the relatives are

TABLE IV.

Blood-pressure of Relatives of Patients with Unclassifiable Toxaemia.

| No. | Father | | | Mother | | | Brothers | | | Sisters | | | Remarks |
|--------|--------|-------------------------|-----|--------|-------------------------|-----|----------|-------------------------|-----|---------|-------------------------|-----|---------------------------|
| | Age | Blood-pressure S. D. | | Age | Blood-pressure S. D. | | Age | Blood-pressure S. D. | | Age | Blood-pressure S. D. | | |
| 578/29 | | | | 83 | 143 | 70 | | | | | | | |
| 51/29 | | | | | | | | | | 44 | 164 | 90 | |
| 203/34 | | | | 74 | 240 | 120 | | | | | | | |
| E 524 | | | | | | | | | | | | | Aunt, 38, 140/72. |
| E 737 | 62 | 160 | 70 | 63 | 200 | 100 | | | | 28 | 132 | 100 | Twins |
| E 690 | 66 | 200 | 100 | | | | | | | 23 | 116 | 92 | |
| E 765 | 58 | 140 | 80 | 53 | 168 | 102 | | | | 28 | 130 | 64 | |
| F 307 | | | | 59 | 180 | 92 | | | | | | | |
| | | | | | | | | | | 35 | 128 | 68 | |
| | | | | | | | | | | 33 | 148 | 74 | Father ill with high B.P. |
| | | | | | | | | | | 33 | 164 | 8 | Twin sisters. |
| | | | | | | | | | | 27 | 130 | 76 | |
| F 250 | | | | | | | 31 | 136 | 74 | 39 | 160 | 90 | |
| | | | | | | | 29 | 176 | 100 | 36 | 180 | 98 | |
| F 229 | | | | 62 | 160 | 100 | | | | | | | |
| F 195 | | | | | | | | | | 26 | 136 | 82 | |
| F 362 | 61 | 210 | 110 | | | | | | | 30 | 132 | 84 | |
| | | | | | | | | | | 25 | 132 | 68 | |
| | | | | | | | | | | 23 | 154 | 96 | |
| F 411 | | | | 42 | 178 | 92 | 19 | 120 | 160 | 22 | 132 | 64 | |
| | | | | | | | | | | 18 | 122 | 64 | |
| F 399 | | | | | | | | | | | | | Twins, aunt, 23, 162/80 |
| F 440 | | | | 51 | 180 | 92 | | | | | | | |
| F 512 | | | | 55 | 182 | 82 | | | | 21 | 116 | 56 | |
| | | | | | | | | | | 19 | 140 | 60 | |
| | | | | | | | | | | 17 | 112 | 48 | |
| F 577 | | | | | | | | | | 49 | 158 | 98 | |
| F 674 | | | | | | | | | | — | 128 | 68 | |
| G 571 | | | | 43 | 176 | 110 | | | | | | | |
| H 41 | | | | 63 | 152 | 80 | | | | | | | |
| H 648 | | | | 51 | 90 | 50 | 34 | 124 | 72 | 36 | 136 | 70 | |
| J 30 | | | | | | | | | | | | | |
| J 346 | | | | 59 | 154 | 90 | | | | 37 | 130 | 80 | |
| J 522 | | | | 63 | 160 | 80 | | | | 33 | 148 | 88 | |
| J 974 | — | 148 | 96 | — | 130 | 70 | | | | | | | |
| K 113 | | | | | | | | | | — | 130 | 80 | |
| L 118 | 52 | 130 | 70 | 52 | 130 | 70 | | | | | | | |
| L 240 | 70 | 170 | 90 | 65 | 150 | 100 | | | | | | | |

hypertensive if the standard of Robinson and Brucer¹⁴ is accepted. Twelve of the 51 brothers and sisters are hypertensive and 37 of the 55 parents. Many of the latter, however, have blood-pressures a very little above normal and a similar incidence of hypertension is found in relatives of control patients.

Table III gives the blood-pressure of 55

relatives of 26 patients with essential hypertension and pregnancy. Here it will be noted that 16 of the 18 mothers of these patients show definite evidence of hypertension, and that in 14 the blood-pressure is markedly raised. The mother of Case A 1359 died of heart disease and asthma and the father also died of heart disease. On the other hand, 2 of the mothers of these

patients had blood-pressures within normal limits (Case C 540, aged 63, blood-pressure 154/64, and Case E 499, aged 51, blood-pressure 130/76). Of the 9 sisters of patients in this group, 4 had blood-pressures well above normal limits, as had 1 of the 5 brothers. These results seem to show that in cases of essential hypertension there is a definite hereditary element, although some of the brothers and sisters have escaped, including the sister of Case A 1359, whose blood-pressure at the age of 44 was only 118/70.

Table IV gives the blood-pressure of relatives of patients with unclassifiable toxæmia. Here the results are similar to those in Table II, with possibly a slightly greater tendency to hypertension. This may be accounted for by the supposition that some of these patients were in fact suffering from essential hypertension.

Table V gives the blood-pressure of relatives of control patients who did not have toxæmia. Here, a similar incidence of hypertension is found to that in relatives of patients with pre-eclamptic toxæmia.

DISCUSSION.

Certain limited conclusions can be drawn from these results. It has been shown that severe pre-eclamptic toxæmia and eclamptic toxæmia and eclampsia do occur in patients in whom it has not been possible to demonstrate a familial tendency to hypertensive disease. This might be expected for other reasons, for example, it is known that eclampsia occurs mainly in first pregnancies and that subsequent pregnancies may be entirely normal. An hereditary factor would be expected to operate in every pregnancy. Also, the incidence of eclampsia is increased in twin pregnancies.

In the cases of essential hypertension and pregnancy, however, it was found that 16

out of 18 of the mothers of patients in this group were severely hypertensive and that the mother of another patient had died of cardiac disease.

On the other hand, when the relatives of patients in the control series were examined it was found that a proportion of them suffered from essential hypertension—some of them to a marked degree. A hypertensive heredity is therefore probably of little importance in the aetiology of toxæmia of pregnancy, except in patients with essential hypertension. It may, however, be of importance in predisposing a patient to permanent hypertension after a pregnancy that has been complicated by pre-eclamptic toxæmia or eclampsia. It was not possible to throw any light on this point, or to obtain any definite evidence on the question of the inheritance of hypertensive disease. The investigation is too incomplete to draw up pedigrees of the various families studied, but, if a hypertensive tendency is inherited on Mendelian lines, and if there is a "gene for high blood-pressure," it would appear that it must be inherited as a Mendelian recessive since some of the children of parents with this disease escape the taint.

Two further points will be discussed briefly. The question often arises whether pregnancy should be terminated in patients who are suffering from benign hypertension. In an earlier paper of ours¹⁶ it was suggested that this is not necessary in the interests of the mother since it has not been proved that a permanent exacerbation of the disease results from pregnancy. In malignant hypertension the picture is very different, and patients with this grave disease should be advised not to become pregnant, or, if conception has occurred, the pregnancy should be terminated. It must be noted that many of the mothers of patients in this series had reached the age of 60 or even 70 with severe hypertension,

TABLE V.

Blood-pressure of Relatives of Patients who had no Toxaemia (Controls).

| No. | Father | | | Mother | | | Brothers | | | Sisters | | | Remarks |
|--------|--------|-------------------------|-----|--------|-------------------------|-----|----------|-------------------------|----|---------|-------------------------|----|----------------------------|
| | Age | Blood-pressure S. D. | | Age | Blood-pressure S. D. | | Age | Blood-pressure S. D. | | Age | Blood-pressure S. D. | | |
| E 587 | | | | | | | 22 | 122 | 64 | | | | |
| E 245 | | | | 63 | 170 | 100 | | | | | | | |
| E 302 | | | | | | | | | | 26 | 140 | 88 | |
| B 487 | | | | 64 | 152 | 66 | | | | | | | |
| E 118 | | | | | | | | | | 46 | 136 | 70 | |
| E 300 | | | | | | | | | | — | 140 | 80 | |
| E 343 | | | | | | | | | | — | 140 | 80 | Aunt, B.P. 124/88 |
| E 551 | | | | — | 140 | 80 | | | | | | | |
| E 521 | | | | | | | | | | 29 | 116 | 70 | |
| E 440 | — | 176 | 88 | — | 158 | 84 | | | | 26 | 118 | 68 | |
| F 113 | | | | | | | | | | 20 | 136 | 72 | |
| F 544 | 49 | 138 | 62 | 48 | 138 | 72 | | | | | | | |
| F 716 | | | | | | | 30 | 124 | 70 | | | | |
| G 21 | | | | 51 | 164 | 84 | | | | | | | |
| G 73 | | | | 40 | 110 | 78 | | | | | | | |
| G 29 | | | | | | | | | | 30 | 120 | 70 | |
| G 31 | | | | 52 | 130 | 80 | | | | | | | |
| G 106 | | | | 53 | 140 | 90 | | | | | | | |
| G 418 | | | | 51 | 220 | 130 | | | | 19 | 116 | 54 | Father died, heart failure |
| G 607 | 50 | 160 | 70 | 50 | 140 | 64 | | | | | | | |
| A 237 | | | | 60 | 120 | 60 | 23 | 120 | 60 | | | | |
| C 868 | | | | 64 | 160 | 110 | | | | 31 | 138 | 80 | |
| | | | | | | | | | | 18 | 128 | 78 | |
| G 549 | | | | 69 | 210 | 100 | | | | 33 | 124 | 62 | |
| G 505 | | | | | | | | | | 33 | 122 | 68 | |
| F 544 | 49 | 138 | 62 | 48 | 138 | 72 | | | | | | | |
| G 550 | | | | | | | | | | 33 | 120 | 70 | |
| G 574 | | | | 51 | 140 | 80 | | | | | | | |
| G 531 | | | | 55 | 118 | 64 | | | | | | | |
| G 577 | | | | 52 | 164 | 96 | | | | | | | |
| G 681 | — | 126 | 80 | — | 118 | 72 | | | | — | 118 | 68 | |
| F 58 | | | | 61 | 170 | 100 | | | | | | | |
| G 580 | | | | 51 | 140 | 76 | | | | | | | |
| H 22 | | | | 41 | 128 | 72 | | | | | | | |
| H 36 | | | | | | | | | | 28 | 110 | 56 | |
| H 38 | | | | 58 | 150 | 110 | | | | | | | |
| H 47 | | | | 43 | 120 | 78 | | | | | | | |
| H 42 | | | | 50 | 136 | 78 | | | | | | | |
| H 65 | | | | | | | | | | 42 | 138 | 60 | |
| | | | | | | | | | | 40 | 140 | 78 | |
| | | | | | | | | | | 38 | 122 | 64 | |
| H 66 | | | | 61 | 148 | 82 | | | | | | | |
| H 122 | | | | 46 | 170 | 86 | | | | | | | |
| H 148 | | | | | | | | | | 34 | 116 | 80 | |
| H 401 | | | | | | | | | | 30 | 112 | 70 | |
| H 531 | | | | 70 | 220 | 90 | | | | | | | |
| E 29 | | | | — | 86 | 50 | | | | — | 114 | 66 | |
| H 746 | | | | 72 | 194 | 82 | | | | 34 | 80 | 50 | |
| J 1004 | 61 | 162 | 104 | 50 | 158 | 75 | 28 | 132 | 88 | | | | Uncle died of high B.P. |
| K 158 | | | | | | | 36 | 130 | 80 | 38 | 122 | 70 | |
| | | | | | | | 32 | 126 | 72 | | | | |

which might have been present, undetected, during their pregnancies and was often revealed for the first time at this examination.

The second question is whether patients with benign hypertension should be discouraged from having children on eugenic grounds. Clearly there is little in favour of this. The evidence of hereditary transmission of this disorder is, as yet, not based on any reliable statistical evidence, and in any case the severe manifestations are unlikely to occur before late middle age or even senescence.

Maurice Campbell⁴ summed up the situation as follows:

"Only exceptionally when these conditions (cerebral haemorrhage, angina, etc.) have occurred frequently and at an early age are we justified in warning against parenthood. Practically our advice is limited by the fact that cardiovascular disease is likely to occur in those stocks which are desirable from other points of view, that is to say, in their freedom from more important disabilities like tuberculosis and mental disorders. If a disease does not occur before sixty or later its occurrence may be no contra-indication to parenthood, even if it were known to be inherited with certainty, especially as the vigorous and capable type in whom cardiovascular disease is likely to occur may have excelled in almost any walk of life before the age at which the malady manifests itself."

CONCLUSIONS.

1. It is well known that a tendency to high blood-pressure may be inherited though the evidence for this is based on records of individual families rather than on statistical study.

2. Many individual reports have appeared of the occurrence of eclampsia in several members of the same family. A tendency to hypertensive disease in rela-

tives of patients suffering from eclampsia and pregnancy toxæmia has also been noted.

3. The blood-pressure has been recorded in 226 relatives of 129 patients who were admitted to hospital with pregnancy toxæmia. These patients have been divided into 4 groups: Eclampsia, pre-eclamptic toxæmia, essential hypertension and pregnancy, and unclassifiable toxæmia.

4. The blood-pressure was also estimated in 66 relatives of 47 control patients who were not suffering from toxæmia.

5. A demonstrable difference in the levels of blood-pressure has not been noted between the relatives of toxæmic and control patients, except in cases of essential hypertension and pregnancy. Here it was found that 16 among 18 mothers of the patients in this group were markedly hypertensive.

6. It is concluded that there is not any evidence that a hereditary tendency to hypertension is of any general importance in the aetiology of toxæmia of pregnancy except in cases of essential hypertension and pregnancy.

7. The implications of these findings are briefly discussed, and it is concluded that it is rarely necessary to interrupt pregnancy in a case of essential hypertension in the interests of the mother. Nor should patients with a familial history of hypertensive cardiovascular disease be discouraged from having children, except in those very rare cases in which the manifestations of the disease have occurred frequently and at an early age.

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The Prevention of Premature Labour

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INTRODUCTION.

NEVER before has the problem of a declining birth-rate attracted such attention as now. Obviously it is not enough for us to prolong the expectancy of life of the living. To survive as a nation in this competitive world we must also salvage more life at its source. Whitton¹ has recently pointed out that in Canada, in 1921, there were 75 persons over 60 years old and 240 under 10 years old, per 1,000 population. But in 1941, only 20 years later, there were fully 102 persons in the older group pyramided on a shrinking base of 182 in the juvenile group. Thus, prevention of abortion and miscarriage, and the conservation of the premature infant, once interests of the obstetrician only, now cast their medical robes like Phrygne and stand forth in the politico-economic arena. These really are matters of national life and death.

The enormous annual wastage of lives during the neonatal period, too, has recently been commented upon by many authors. Potter,² for instance, points out that, in spite of steadily improving obstetric practice in the United States, there has been but very slight decrease in the deaths occurring under the age of 1 day since 1937 (15.1 deaths per 1,000 live births in 1927, as compared with 13.9 per 1,000 in 1940). Admittedly, mortality within the 1st month, during the same period of years, has

decreased somewhat more rapidly—from 35.5 deaths per 1,000 (1927) to 29.0 per 1,000 (1940)—but that also is still too high.

That the problem is acute is evidenced further by an aggregate of 144,692 foetal and neonatal deaths in the United States in 1941, the last year for which statistics are yet available. As Sage³ comments, this is more than the total number of deaths among all persons in the age-group of 5 to 29 years, and constitutes fully 10.4 per cent of the total deaths from all causes. Sandifer⁴ shows that in England and Wales "prematurity" caused more deaths in 1938 than "coronary disease" or "old age," about as many as were due to "tuberculosis," and about one-third as many as "cancer." Most large hospitals in the United States and Britain report that 5 to 10 per cent of all births are premature. Peckham⁵ could not find any significant improvement in the prematurity figures of the Johns Hopkins Hospital in the 40 years prior to 1936. Schwartz,⁶ of the Children's Bureau, U.S. Department of Labour, Washington, writes that the estimated number of premature births in the United States in 1942 was 155,000, and that 33,500 premature infants died in the 1st month of life. Marshall⁷ of the Dominion Bureau of Statistics, Ottawa, mentions that in 1940 there were 12,268 premature babies born in Canada, amounting to 5 per cent of the live births. There were fully 3,340 stillbirths ascribed to prematurity, amounting to 54 per

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cent of all the stillbirths where the period of gestation was stated; 2,000 deaths in the 1st month of life were ascribed to prematurity. To put it in another way, 50 per cent of all premature babies born in Canada in 1940 were dead at birth, or died in their 1st month. But it should be pointed out that in the whole European theatre of the war, in 5 years and 8 months of fighting, Canadian losses in killed and missing amounted to 40,975 among over 1,000,000 enlistments, a mortality of 4 per cent. It is, therefore, more than 12 times as dangerous for a premature infant to be born in Canada as it was for a Canadian man to enlist in the war. And if we take 1940 as a representative year, then during the war Canada lost 35,360 premature babies, almost as many citizens as she lost by enemy action. Is prematurity a vital Canadian problem? One suspects the truth is that, if there had not been any premature children born during the war, the population in that time would not have been decreased. And we are speaking only of prematurity and ignoring spontaneous abortion and miscarriage, which kill at least as many potential citizens.

In Chicago, Bundesen and his co-workers⁸ found prematurity to be the largest single cause of neonatal death in a series of 1,043 necropsies. Intracranial haemorrhage and malformations came next in order of frequency — and, of course, prematurity contributed to a fair proportion of these deaths as well.

The death-rate in infants born too soon appears to vary directly with the degree of their prematurity. Dunham⁹ demonstrated that, of foetuses born weighing less than 1,000 grams (2.2 pounds), 95 per cent succumbed; of those from 1,000 to 1,500 grams (2.2 to 3.3 pounds), 72 per cent; of those from 1,501 to 2,000 grams (3.3 to 4.4 pounds), 32.5 per cent; while of those weighing from 2,000 to 2,500 grams (4.4 to

5.5 pounds), only 8.7 per cent perished. Studies made in New York City¹⁰ and New York State¹¹ indicate that prematurity doubles the neonatal mortality. Still more startling is the calculation of Potter and Adair¹² that the combined neonatal mortality and stillbirth-rate of premature infants amounts to 18 times that of babies born at term. The practical relation of this problem to national survival surely becomes strikingly apparent.

In Chicago, a determined effort has been made in recent years to lower the death-rate of newborn infants. For example, in the 4 years from 1936 to 1940 the death-rate of premature babies under 15 days was reduced by 15 per cent and of all infants by 25 per cent.¹³ This result is significant, of course, but when one knows the nature of the intensive measures Hess, Bundesen, and others adapted in their life-saving campaign, it can readily be seen that not much more can be hoped for by such efforts and that the solution of the problem does not lie in saving premature infants but rather in preventing premature births. A very good summary of the whole problem is given in the Report on Infant Mortality in Scotland for 1943.¹⁴ The dietary experiments carried on at Toronto¹⁵ and elsewhere suggest that dietary improvement decreases the actual incidence of prematurity, and this was borne out by a vitamin E study¹⁶ published in 1942.

In 1937, it was suggested by one of us (E.V.S.¹⁷) that the mechanism of premature labour might be initiated by an abnormality similar to that causing spontaneous abortion and miscarriage, as might be expected on *a priori* grounds. Developmental anomalies figure unduly prominently in any series of premature births, and further substantiate the impression that the causes of abortion and prematurity may be much the same. Sandifer⁴ brings out clearly the relation that has long been obvious between

the occurrence of prematurity and maternal toxæmia, antepartum hæmorrhage, or multiple pregnancy. Apart from the group of congenital anomalies, there remained a large group in his study where the cause of the prematurity was not found and was therefore potentially discoverable.

DATA.

We present below a tabulated series of 63 consecutive, unselected cases of threatened and actual premature labour compiled from the practice of both authors and our colleague, Dr. Mary Wong, investigated by similar criteria and identically treated. Our results are as follows:

TABLE A.—Cases terminating in normal living infants at term.

| Number of cases | Previous abortions or other abnormal terminations of pregnancy | Blood oestrogen | | | Average time when labour first threatened | Symptoms | | | Weight of infants |
|-----------------|--|-----------------|---------------|-------------|---|----------|---------------|--------|-------------------|
| | | Posi- tive | Nega- tive | Not done | | Mild | Mode- rate | Severe | |
| 37 | 9 | 20 | 1 | 16 | 32 weeks | 20 | 4 | 13 | 7 lb. 7 oz. |

TABLE B.—Cases terminating in normal living infants 38 weeks or younger.

| Number of cases | Previous abortions or other abnormal terminations of pregnancy | Blood oestrogen | | | Average time when labour first threatened | Symptoms | | | Weight of infants (excluding twins) |
|-----------------|--|-----------------|---------------|-------------|---|----------|---------------|--------|-------------------------------------|
| | | Posi- tive | Nega- tive | Not done | | Mild | Mode- rate | Severe | |
| 21 | 10 | 9 | 4 | 8 | 33 weeks | 7 | 2 | 12 | 5 lb. 2 oz. |

TABLE C.—Cases terminating in stillborn infants.

| Number of cases | Previous abortions or other abnormal terminations of pregnancy | Blood oestrogen | | | Average time when labour first threatened | Symptoms | | | Weight of infants |
|-----------------|--|-----------------|---------------|-------------|---|----------|---------------|--------|-------------------|
| | | Posi- tive | Nega- tive | Not done | | Mild | Mode- rate | Severe | |
| 5 | 1 | 4 | 0 | 1 | 31 weeks | 5 | 1 | 1 | ? |

DISCUSSION.

If we define prematurity by the criterion of 5½ pounds (2,500 grams) weight and more than 28 weeks of gestational age,

even better than is suggested by the above figures, can be made out for the regimen we have used in treatment.

If it be objected that not all the patients

there was a salvage in this series of 46 cases, or 73 per cent. If we add to this the 46 cases reported in the previous publication on this topic referred to above,¹⁵ it will be seen that the salvage amounted to at least 72 per cent. This represents a considerable number of lives saved, and such figures could no doubt be greatly improved had we felt free to use as large doses of vitamin E as we desired, without regard to its cost, and had we seen some of these patients earlier in their precarious pregnancies. Some of the very small babies have survived too, and others were anomalous and beyond the power of anyone to preserve. It is obvious that a good case,

listed here were threatening premature labour, we may select the obviously severe threats, and those first seen during labour, numbering 28 in all. Of these, 21, or 75 per cent, were preserved, an almost identical rate of salvage. If it be pointed out that there are too few induced premature labours mentioned here, and that that unduly favours our thesis, we may reply that we control our toxæmias so well that all go to term or near it, being ambulant throughout, and that the average birth-weight of our non-eclamptic late toxæmia babies is half a pound above the normal.¹⁴ In this series, however, 4 cases were induced, 1 for very severe recurrent pyelitis and 3 for toxæmia. Even in these 4 cases the same percentage of salvage holds. It would seem, therefore, that 3 of every 4 babies threatened with premature expulsion can be preserved.

In this study it was found that a tendency to premature labour could usually be predicted by finding a blood-oestrogen excess even in early pregnancy, confirming an observation reported¹⁷ several years ago. That it occurred in 87 per cent of the 38 cases tested, can hardly be termed accidental. It is of interest that Hall,¹⁸ using a vaginal smear method, has recently observed that oestrogen excess precedes abortion and miscarriage. In many of our patients symptoms of threatened abortion or threatened miscarriage had previously appeared, but these had subsided promptly on instituting vitamin E therapy or increasing the dose already being given. Such management appears to have allowed many cases, otherwise precarious, to carry through to term. However, only a large daily dose—75 to 125 mg. of Alphatocopherol—can save the situation sometimes, for if too high a tide of oestrogen undermines the piers the uteroplacental bridge goes down. There must be vigorous and adequate treatment with a potent vita-

min E preparation until term. Even at this late date in vitamin E therapy it is discouraging to discover that many or most physicians employ cheap and relatively impotent products masquerading as good vitamin E—to the unduly prolonged discredit of this type of treatment.

Frequently premature labour begins, almost unheralded otherwise, with rupture of the membranes. Many a patient, too, forgetting her physician's warning, reports to him several hours after the onset of pains when labour has unmistakably set in. Thus, a valuable opportunity may be lost and delivery become inevitable before preventive treatment can be undertaken. It takes almost 24 hours, unfortunately, for vitamin E to control a case.

Accordingly, we stress the importance of a routine blood-oestrogen test at the patient's first antenatal visit. We thus have a gauge of the dangers ahead, and can institute daily prophylactic therapy with vitamin E as indicated. Indeed it can do no harm, unless the woman is a true pre-eclamptic, to give vitamin E to every pregnant patient until at least the 8th month. If, in spite of this management, the patient temporarily escapes from control, larger supplementary doses may quickly be given in order to restore the normal balance.

As pregnancy progresses the enlarging placenta requires a gradually increasing amount of vitamin E to maintain its "cling" to the uterus. This adjustment of dosage is largely a matter of judgment and experience. An eye alert to detect early symptoms of trouble is essential. It may save much later anxiety and win many a battle before the first shot is fired. Accordingly, each patient is warned to report an area of uterine tenderness, or sacral back-ache, or spotting of blood, or loss of amniotic fluid, or a feeling of prolapse or impending menstruation. These mean that she is escaping from vitamin E control.

A study of consecutive pregnancies suggests a definite trend towards repetitive behaviour.¹⁹ Once the "abortion sequence" of Young²⁰ is established, abortion, or miscarriage, or abruptio placentae, or a late toxæmia, or premature labour tend to recur in later pregnancies. Each pregnancy seems harder to carry to term than its predecessor. It should be emphasized that an unstable pregnancy does not necessarily mean a defective infant, in spite of much opinion to the contrary. Of the 109 pregnancies in this and the previous reported groups, only 5.5 per cent terminated in the delivery of malformed children, and only 1 of these 6 with a cleft palate lived for more than 3 months. Could anything argue more clearly that the remaining 92 had a claim to salvage? Some years ago the data in the literature on all threatened abortions saved by the use of vitamin E, or progesterone or both was summarized,²¹ and only 3 per cent were found to have resulted in anomalous infants.

SUMMARY.

1. A series of 63 cases of threatened premature labour is presented. Of these 73 per cent were salvaged.

2. Of the patients in this group on whom a blood-oestrogen was done, 87 per cent showed a high blood-oestrogen, even early in pregnancy.

3. The only therapy used was vitamin E, with or without temporary rest in bed.

4. The importance of using a vitamin E preparation of reliable potency, both in adequate dosage and until term, is emphasized again.

5. Of the 109 patients included in this and our previous report, there were 6 monsters delivered, only 1, with a cleft palate, surviving over 3 months. But 92

normal living children were obtained. Their preservation would seem justifiable.

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Carcinoma Corporis Uteri in 2 Sisters Aged 34 and 32 Years

BY

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In a prior communication¹ the occurrence of carcinoma corporis uteri in each of 2 sisters, aged 34 and 32 years respectively, was described briefly. Interest and scepticism were aroused. One eminent gynaecologist wrote to me: "I, personally, am deeply convinced that this condition *never* occurs before the menopause. . . . My mind, however, is quite open to be convinced that carcinoma corporis does occasionally occur before the menopause, and I would therefore be very grateful if you would send me a complete range of your sections in order that I may endeavour to convince myself."

This was done. After studying the material he replied: "I am wholly convinced that the sections show a definite carcinoma of the body of the uterus. I have to-day discussed these sections with our Professor of Pathology and he can recall only 1 other case in a woman before her menopause in his large experience." It is probable that others were equally sceptical. It is obviously important to establish the fact that corporeal carcinoma does occur, even if only occasionally, long before the menopause. Adenocarcinoma of the uterine body is an eminently curable condition if recognized sufficiently early. It is to be regretted that many subjects of malignant disease fail to seek advice until the condition is so advanced that all hope of cure is gone. But how much greater the regret if the patient seeks advice early and the condition is not recognized because the attendant doubts the possibility of its

existence. It has been decided, therefore, to present the cases in more detail with microphotographs to substantiate the diagnosis.

A complete review of the literature of premenopausal corporeal carcinoma has not been attempted, but a sufficient number of cases is cited to show that it can and does occur. The importance, then, of diagnostic curettage, even in young women who have prolonged or irregular uterine bleeding, should require no emphasis. In the case of my 2 patients there is the added interest of their being sisters.

CASE HISTORIES.

Sister No. 1.

Aged 34 years; nullipara; married 10 years, during which contraception has been practised constantly. Admitted to the North Middlesex County Hospital on April 4th, 1940, for severe vaginal bleeding of 10 days' duration. There had not been preceding amenorrhoea.

Menarche aged 15 years. Until about 28 years of age the periods were regular, lasting 3 days and recurring every 4 weeks. Then the menstrual loss became more profuse, lasting 3 to 7 days, recurring every 4 weeks. For 2 years prior to admission the loss was greater still, lasting sometimes even 14 days. Coital bleeding occurred occasionally during those 2 years. There have been irregular haemorrhages recently. The patient has never experienced dysmenorrhoea or dyspareunia. For years she has had a profuse white vaginal discharge. This discharge has been like "muddy water" for about 2 years prior to admission. There has been constant backache.

At 24 years of age a right-sided ovarian cyst, weighing 24 pounds, was removed at another hospital. (This cyst had not caused any menstrual disturbance.)

On examination the general condition was good. The breasts did not show changes suggestive of pregnancy. The abdominal findings were normal except for a long paramedian scar. But for slight uterine enlargement the pelvic findings were normal. Curettage was performed. Macroscopically the curettings suggested incomplete abortion. Microscopically this condition was excluded. The possibility of malignancy was considered, but, in view of its improbability, it was decided to postpone judgment and to keep the patient under careful clinical review.

Normal menstruation continued, except that in August there was bleeding for 1 month. In November and December bleeding became irregular, and a second curettage in January 1941 showed endometrial carcinoma. Total hysterectomy with left salpingo-oophorectomy was performed (the right ovary had been removed previously, *vide supra*) and followed by deep X-ray therapy. The patient made an uninterrupted recovery. The uterus on section showed endometrial carcinoma invading the wall. The ovary and tube did not show involvement by the growth.

The histological material of this (and of the subsequent) case has been recently submitted to Dr. I. Doniach, whose reports are incorporated in this paper.

Histology (I. Doniach).

First Curettings (April 4th, 1940). There is a gross glandular hyperplasia consisting of closely packed convoluted acini lined by more than one layer of cells. Some acini show numerous mitoses and their lumina are filled with polymorphs. The picture is strongly suggestive of adenocarcinoma.

Second Curettings (January 7th, 1941). The acini are even more closely packed, solid and made up of atypical cells. This is a definite adenocarcinoma.

Uterus (January 17th, 1941). (Figs. 1 and 2). This is a polypoid adenocarcinoma showing malignant infiltration of the endometrial stroma, but only slight infiltration of the myometrium. The glands away from the growth show the cystic dilatation seen in metropathia haemorrhagica.

Sister No. 2.

Aged 32 years; nullipara; married 9 years; no contraception. Admitted to the North Middlesex County Hospital on October 16th, 1942, because of severe vaginal bleeding for 1 week. There had not been preceding amenorrhoea. Menarche at 13 years of age. The periods have never been very regular. The menstrual flow has lasted from 6 to 10 days and recurred every $3\frac{1}{2}$ to 4 weeks. Upon a number of occasions the patient has suffered from menorrhagia with increased irregularity in the length of the cycle. She has attended the gynaecological out-patient department of 2 other hospitals because of this, but curettage has not been performed. The period in September 1942 was very heavy. While coital bleeding has never occurred, dyspareunia has been present from time to time. She has never experienced any dysmenorrhoea. There has been slight vaginal discharge intermittently over a period of years.

On examination the general condition was good. The breasts did not show signs of pregnancy. Abnormality was not noted on abdominal or pelvic examination. Diagnostic curettage was performed and yielded a piece of tissue suggestive either of incomplete abortion or corporeal carcinoma. Histology proved it to be the latter. Total hysterectomy with bilateral salpingo-oophorectomy was performed, followed by deep X-ray therapy. Convalescence was normal.

Histology (I. Doniach).

Curettings (October 19th, 1942). (Fig. 3). These consist of fragments of a moderately well differentiated columnar-celled adenocarcinoma, arranged in closely packed acini lined by multi-layered atypical cells. Many show a small lumen. Others are distended with mucoid material. Mitoses are abundant. In some areas the stroma is infiltrated with polymorphs.

Uterus (October 23rd, 1942). (Fig. 4). This contains a polypoid endometrial adenocarcinoma showing malignant infiltration of the stroma and subjacent myometrium.

Both patients have been followed up regularly. They have remained well and free from any sign of recurrence. They were last seen in September 1945. On this occasion blood was taken from each sister for Rh typing. In each the blood is group O(4). Sister No. 1 is Rh positive, while Sister No. 2



FIG. 1.

Section of uterus after hysterectomy (Sister No. 1)
Microphotograph $\times 25$.

A.W.P.

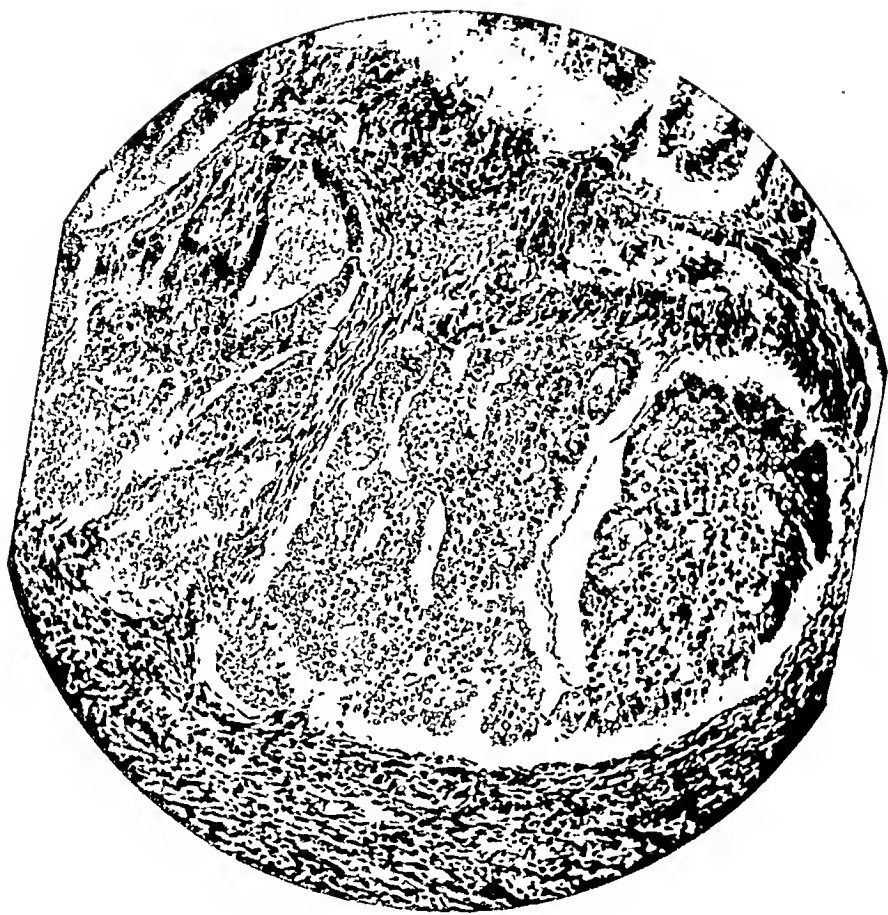


FIG. 2.

Section of uterus after hysterectomy (Sister No. 1)

Microphotograph $\times 100$.

A.W.P.

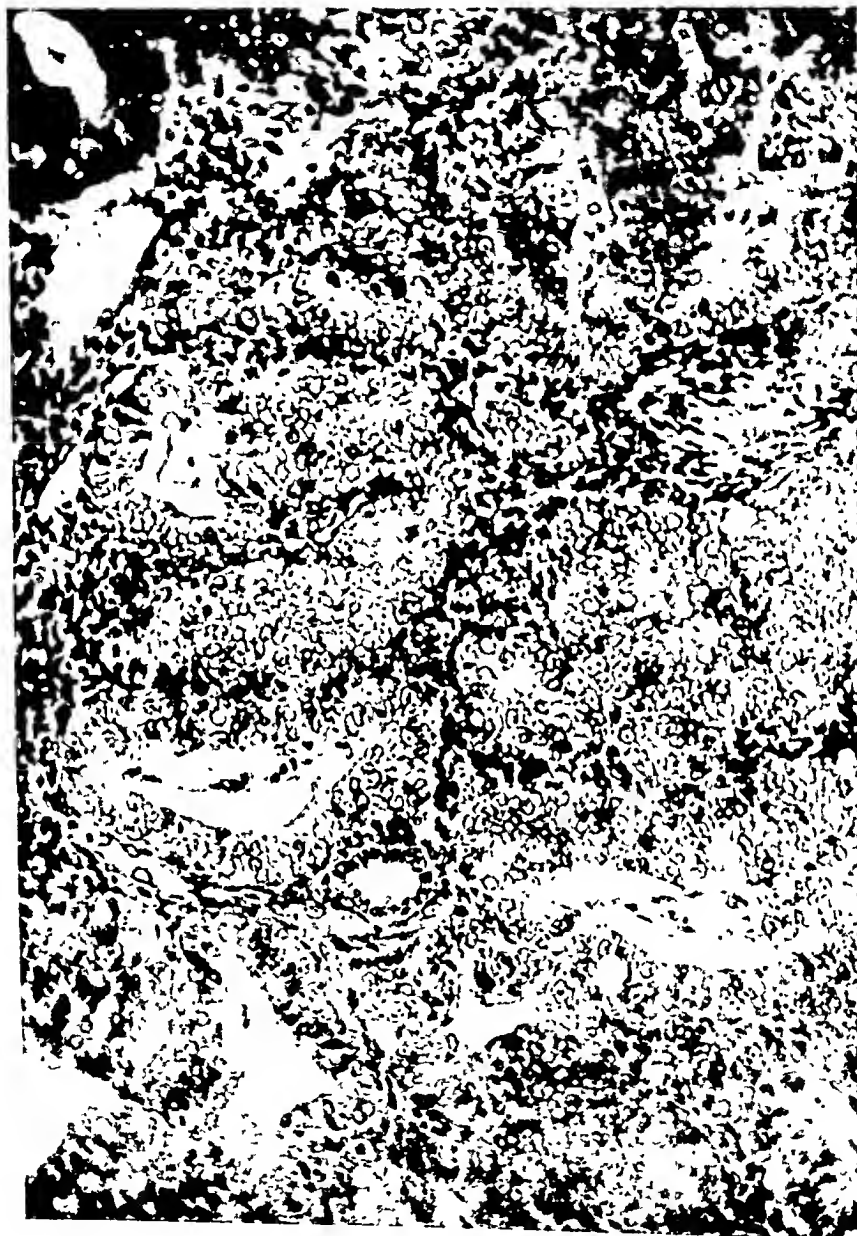


FIG. 3.

Section of curettings (Sister No. 2).

Microphotograph $\times 240$.



FIG. 4.

Section of uterus after hysterectomy (Sister No. 2)
Microphotograph $\times 135$.

is Rh negative. In neither case did the serum contain Rh antibodies.

The patients' mother had 10 children. One sister died of meningitis at 10 months of age. The rest are alive and well. Recently another sister (Brews²) has undergone hysterectomy for a benign condition. The mother died of cancer of the rectum aged 68; and 2 maternal uncles died of cancer of other organs.

In view of a possible milkborne carcinogenic factor (Bitner³) inquiries were made into the early feeding of the 2 sisters who were my patients. From elder members of the family it was learned that they were fed artificially as "their mother never had any milk."

DISCUSSION.

Corporeal carcinoma is typically a post-menopausal condition. In series of any size (Norris and Dunne⁴; Crile and Elias⁵; Masson and Gregg⁶) the largest number of cases occurs in the 6th decade of life. Many observers find the average age of incidence to be within the narrow limits of 56 to 58 years. While this may be so, a small but appreciable number of cases is encountered in the 4th decade (Beattie⁷, 3 per cent.; Crile and Elias⁵, 4 per cent.; Morrin and Max⁸, 4.5 per cent.; Healy and Brown⁹, 3 per cent.; Masson and Gregg⁶, 3.5 per cent.; Brindley¹⁰, 3 per cent.; Barns¹¹, 3.16 per cent.). From time to time it is met with at the age of 19 or 20 (Smith¹²; Morrin and Max⁸; Healy and Brown⁹; Kenny¹³).

Of great interest is its occurrence in children. Hirst¹⁴ saw a girl of 15 years of age who, 5 months previously, had had a cervical polyp removed. He excised the stump of the polyp and fulgurated the base. Eleven months later the patient returned with profuse bleeding. Another polyp was avulsed, and the uterus curetted. Histology showed corporeal adenocarcinoma. Total hysterectomy with bilateral salpingo-oophorectomy was performed. Ten months later the patient was alive and

well. Morse¹⁵ quotes Kehler and Nennmann, who described the occurrence of corporeal uterine carcinoma in a child aged 16 months. Necrotic purulent material escaped during the extirpation of the tumour, and the child died 10 days later of peritonitis. Gilbert¹⁶ performed fundal hysterectomy with right salpingo-oophorectomy in a girl of 11 years of age 6 months after the onset of vaginal bleeding. The specimen showed corporeal carcinoma. In spite of deep X-ray therapy she developed extensive metastases in the chest and died 9 months after operation. Others have described uterine cancer in children but these appear to have been cervical carcinomata. Shaw¹⁷ described a case of adenocarcinoma of the uterine cervix in a girl of 15 years, and reviewed the literature of cervical carcinoma in children and adolescents. He found 12 cases in which he considered it established that the cancer had originated in the uterine cervix. Morse¹⁵ described a very cellular adenocarcinoma of the genital tract in a girl aged 10 years. He considered it to be cervical in origin, but states that Ewing thought it had arisen from a foetal rest in the pelvic cavity.

The other aspect of the matter is familial occurrence. In considering a familial tendency to cancer we may be interested in its occurrence in any organ of the body; but the tendency to malignant tumours in one organ in members of the same family is of particular interest. Williams¹⁸ tells of a mother and 3 daughters who died of uterine cancer. In another family 3 sisters died of cancer of the uterus at 32, 36 and 53 years of age, as did also their mother and maternal grandmother. Auvray¹⁹ described death from uterine cancer in a grandmother, mother and daughter. All these appear to have been due to cervical carcinomata. Kenny²⁰ has received information that the mother of her young

German-Jewish patient¹³ has recently died, in Asiatic exile at the age of 44, of uterine cancer. She cannot ascertain whether this was corporeal or cervical, but, since suggestive symptoms, such as irregular uterine bleeding, were known to be present in 1939, the probability of corporeal cancer may be entertained.

In the Warthin family, among 174 members reaching the age of 25, 41 persons developed 43 primary carcinomas: 23 of these occurred in females, and of these 23, 15 were uterine corporeal adenocarcinoma: there was not any case of cervical carcinoma in the family (Macklin,²¹ Hauser^{22, 23}). Of the 15 subjects with uterine adenocarcinoma, 6 were under 45, their ages ranging from 39 to 44 years. In only 4 of these was there histological confirmation of the diagnosis. There was only 1 under 40 years of age, and in that case the diagnosis was not confirmed histologically.

Imamura²⁴ claims that if a predecessor with uterine carcinoma transmits the "cancerous diathesis" to her descendants, they are more liable to have the tumour in the uterus than in other organs.

While a familial tendency to carcinoma in the same organ is of speculative interest, the 2 cases described in this paper emphasize a point of great practical importance—the possible occurrence of carcinoma corporis uteri in comparatively young women.

SUMMARY.

(1) It is erroneous to state that corporeal uterine carcinoma never occurs before the menopause.

(2) Two cases of corporeal uterine cancer occurring in sisters aged 34 and 32 years of age are recorded. The diagnosis in each case is substantiated by microphotographs.

(3) That these are not isolated cases is demonstrated by a brief review of the literature.

(4) Cases occur even in childhood.

ACKNOWLEDGEMENTS.

I should like to express my indebtedness to Dr. Herbert Rogers, until recently Pathologist to the North Middlesex County Hospital. It was he who prepared and examined all the pathological material in the first instance, and has helped me in numerous ways since. To Professor James Young of the British Postgraduate Medical School, I am indebted for his interest and to Mr. E. V. Wilmott, A.R.P.S., photographer to the British Postgraduate Medical School, for the excellent micro-photographs which he has produced for me.

Finally, I would thank Dr. I. Doniach, Senior Assistant in Morbid Anatomy, British Postgraduate Medical School, for his kindness in examining and describing these histological preparations for me. I greatly appreciate the placing at my disposal of his wide experience in the histology of malignant disease—particularly in such an instance when it is acknowledged that the subject is controversial.

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Rupture of the Rectus Abdominis Muscle During Pregnancy

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In a recent paper¹ I recorded a case of rupture of the rectus abdominis muscle during pregnancy. The rarity of this complication that a search through the literature discovered only 9 previous instances, my own case making the 10th. Since then 2 more examples have been recorded, by Keevil,² and Liggett,³ in this country. My attention has been drawn lately to a paper by Torpin,⁴ which appeared after my case was recorded. Torpin, in describing his own case, has gone very thoroughly into the literature, and gives a bibliography from which it appears that 28 examples, including his own, have been recorded. This bibliography, however, does not include the cases of Keevil, Liggett and my own, which were all reported just before Torpin's article appeared. The number of cases recorded up to the end of 1943, therefore, is 31. The object of the present paper is to record another instance, which came under my charge in March 1945.

Before giving details of my 2nd case it will be of interest to recall some of the points in the histories of the cases already recorded.

In 18 out of 31 patients there was a history of respiratory trouble, in some of acute onset, in others of a chronic character. In 5 the onset of symptoms coincided with the strain of labour. In 2 there was the history of a fall. One occurred after labour during the course of typhoid fever. Torpin refers to the "special tendency to muscle degen-

eration in typhoid fever and influenza." By far the commonest preceding complication is cough. I drew attention to this in my previous paper, and it is amply confirmed in the literature now studied.

Of the 31 patients, 3 were primigravidae, and 24 were multigravidae, the parity not being stated in 4. Multiparity is therefore a distinct aetiological factor. In 20 cases the onset of symptoms occurred after the 30th week of pregnancy. The stretching of the rectus muscles over the enlarging uterus must therefore play a part.

The difficulty in arriving at the true cause of the symptoms is shown by the fact that in only 8 of the 31 cases was the diagnosis of rupture or haematoma of the rectus muscle made before operation. The other diagnoses ranged through accidental haemorrhage, twisted ovarian cyst, ruptured uterus, pedunculated fibroid, ruptured hydatid of abdominal wall, ruptured liver, appendix, extravasation of urine, hypernephrosis, to no diagnosis at all, the true condition being revealed at laparotomy.

The treatment in 20 cases was operative, with evacuation of the clot and ligation of the bleeding vessel when found, though in many cases a definite bleeding point could not be found. In 4 cases Caesarean section was carried out. In 4 treatment was conservative, and in the others it was not stated.

Four of the patients died. In Torpin's table relating to 28 cases, the ultimate out-

come to the mother is unstated in 6. Four maternal deaths out of 31 patients, however, gives a maternal mortality of 13 per cent. As Torpin rightly says, this condition must rank in danger with the other haemorrhages of late pregnancy.

The foetal mortality is difficult to estimate, owing to the details being incomplete. There were 3 abortions and 5 stillbirths mentioned in Torpin's table. One patient died undelivered. Three others were delivered at the 7th month, including 1 set of twins. It can be safely stated that the foetal mortality-rate is high.

THE PRESENT CASE.

The following is the history of my 2nd case of rupture of the rectus abdominis muscle.

Mrs. S., aged 34, 6-para. Five children were born spontaneously at term, including 1 set of twins. All were alive, the weights being 10, 6, 6½, 9½, and 10 pounds. There was 1 abortion at 4 months. The patient attended the clinic in the 22nd week of the present pregnancy. Prior to the present gestation there was nothing of note in her history, but she stated that she was recovering from a cold. She was booked for delivery at home.

On March 12th, 1945, she was admitted to Mayday Hospital, and was first seen by my assistant. The notes made by him read: "About 33 weeks pregnant. Bronchitis for a week. Abdomen slightly larger in last 2 days. Foetal parts not felt. Cullen's sign present. Uterus extremely tender. Slight loss *per vaginam*. Feels faint. Diagnosis—concealed accidental haemorrhage." I was asked to see her prior to an artificial rupture of membranes being carried out.

I obtained a history of 3 attacks of bronchitis since Christmas, 1944, the last 1 being a week prior to admission. She stated that she had pain in the abdomen with the cough, and that a "long lump came up," which her own doctor saw, and which she located in the position of the right rectus muscle. Later, the pain became severe with coughing.

Examination. Peri-umbilical area much stained

with haemoglobin (Cullen's sign). Whole abdomen tender, but gentle palpation of uterus showed it to be softer than would agree with a concealed accidental haemorrhage producing such definite abdominal tenderness. Also tender just below ribs (i.e., at upper end of right rectus muscle). Vertex felt in lower segment. Foetal heart heard.

It was decided to watch events, and meanwhile the patient was put on a rectal drip of saline and glucose, a 12-hourly pulse and temperature chart was kept, a haemoglobin estimation asked for, and 2 bottles of group O blood were cross-matched. Diagnosis—ruptured rectus abdominis muscle.

The haemoglobin was found to be 40 per cent. Blood transfusion was started. At 4.45 p.m. the pulse-rate had settled from 104 to 84, and she looked and felt much easier. She stated that she had not nearly so much pain as the previous night, and much less than when she came into hospital. Abdomen less tender, and now mostly in the right rectus region.

At 6.0 p.m. she vomited. The pulse-rate rose to 112; she complained of feeling cold, looked shocked, and the picture was typical of an internal haemorrhage. The abdomen was not more tender, and foetal parts could be easily felt in the left side of the abdomen. In view of the deterioration in the condition, operation was decided on.

Under general anaesthesia a right pararectal incision was made. On deepening it, considerable bloodstaining of the subcutaneous tissues was seen, mainly in the umbilical region. On opening the right rectus sheath, large clots were seen between the inner edge of the rectus muscle and the posterior sheath. Fresh and old blood clots of the amount of 30 ounces were removed from the whole length of the posterior aspect of the rectus muscle, extending up to the right costal margin and down to the symphysis pubis. Clots were also removed from the right loin, the hand being passed outwards almost to the level of the iliac crest. To reach this situation the blood must have passed beneath the lower free edge of the posterior sheath of the muscle, and outwards between the peritoneum and the transversalis muscle. After clearing the blood from below the semilunar fold of Douglas, the uterus and some omentum could be plainly seen through the peritoneum, there not being any sign of intra-peritoneal bleeding. The right rectus muscle was in the main intact, but its deep surface at the level

of the umbilicus was somewhat broken up, and a branch of the deep epigastric artery was found to be torn and still bleeding. This was ligatured. Another smaller vessel was found higher up, and this was also tied. A large pack was then placed along the whole length of the deep surface of the muscle, the lower end being brought out through the lower end of the incision, which was then closed, with tension sutures placed about every $1\frac{1}{2}$ inches to guard against bursting of the wound through coughing. The patient was very chesty during the operation.

During the next few days the general condition improved, but the cough was very troublesome, much purulent sputum being brought up. Atropine gr. $\frac{1}{200}$, 4-hourly, and Transpulmin twice daily were given. Fluids were not taken very well by mouth, and there was some vomiting. The quantity of urine passed during the first 3 days was small, but the significance of this was clouded by the general condition. Intravenous and rectal salines with glucose were given to make up for the poor oral intake.

On March 17th, the 5th day after operation, the woman came into labour, and a stillborn female infant, weighing 3 pounds 12 ounces was delivered, the presentation being a breech. Unfortunately, there was a loss of 58 ounces before the placenta was delivered. Further transfusion of 2 bottles of group O blood was given after cross-matching. Towards the end of this she had a rigor and became very restless. Urinary output practically ceased, only 8 ounces being passed during the next 5 days. A severe degree of jaundice also ensued, and the next 10 days were spent in a fight against anuria due to the incompatible transfusion. The clinical details of her condition during this period will be reported in a further paper. It must suffice to say that after about 10 days, during which she was given 2 further transfusions of Rh negative blood totalling 4 pints, she began to pass urine in increasing amounts, her general condition, apart from the jaundice and the anuria, remaining remarkably good. After a sharp attack of Bact. coli pyelitis, which yielded quickly to sulphathiazole, she made a complete recovery, and was discharged on April 28th, the 47th day after admission. The abdominal incision was firmly healed, and the right rectus muscle appeared to be functioning well. There was no abdominal tenderness.

SUMMARY AND COMMENTS.

A case of rupture of the rectus abdominis muscle during pregnancy is recorded, the 2nd example to be seen by me, and the 32nd disclosed in the literature.

In the aetiology, multiparity and the strain on the rectus muscles entailed by persistent cough, play the major parts. Other factors are the strain of labour, trauma such as a fall, and in 1 case muscle degeneration due to general disease. All the cases reported have been in the 2nd half of pregnancy, the majority being within 8 weeks of term. Stretching of the rectus muscles by the enlarging uterus must also be a factor.

The difficulty in diagnosis is shown by the great variety of wrong assumptions prior to operation. In only 9 out of 32 cases was the correct diagnosis made.

In 5 instances Cullen's sign was present. The significance of this sign, if the possibility of haemorrhage into the rectus sheath is borne in mind, is obvious.

The condition carries a maternal mortality of 13 per cent, and a foetal mortality probably in the region of 50 per cent. It must, therefore, rank with the other haemorrhages of late pregnancy in danger to mother and child.

The number of cases reported would seem to imply that the condition is rare. Torpin states that "probably a great number of haematomas of the rectus muscles in pregnancy and labour are small, unnoticed and undiagnosed, and consequently unreported." This is probably true, and it is noticeable in the literature that a number of cases have been diagnosed as "concealed accidental haemorrhage." It is very likely that some cases so diagnosed, and treated by artificial rupture of the membranes, have been delivered and have recovered without the true cause ever having been revealed.

In regard to treatment the literature shows that 21 patients were operated upon, with evacuation of the clot, and that in 3 instances the bleeding vessel was found and ligatured. In 4 of these cases Caesarean section was also performed. Torpin's study of the literature led him to the conclusion that conservative treatment is indicated, the chief of these being early diagnosis, complete rest, and blood transfusions when indicated. Torpin's notes of his own case show that on admission the patient had a normal pulse and temperature, physical findings were quite normal except in the abdomen, where there was a mass the size of a large grapefruit rather firm and tender. He goes on to say that the "correct diagnosis was not made, probably because it was not thought of. The following were considered: ovarian cyst, fibromyoma, hydronephrosis, and finally after ecchymosis of the skin appeared, simultaneous intrauterine and ectopic pregnancy. The condition being not very disturbing she was observed for 2 weeks. After some improvement she was allowed to walk around. This was followed by an increase in pain and the size of the mass. Finally, late in the 2nd week, there appeared an area of extravasation of blood into the skin below the umbilicus, further increase in the tumour, and mild surgical shock with sweating and prostration. Her symptoms indicating severe haemorrhage an exploratory laparotomy was done." Only then was the true cause ascertained.

It seems to me that conservative treatment is only justified so long as the general condition remains good and there is no increase in the size of the tumour or of the abdominal pain. If the symptoms point to increase in haemorrhage, shown

by rising pulse-rate, pallor, shock, increase in pain and the size of the tumour, I feel that operative intervention has now become urgent, an opinion which is surely supported by the known mortality of 13 per cent. It must be remembered that the blood can find its way between the abdominal muscles and the peritoneum, where enough can accumulate to be rapidly fatal, or can even rupture into the general peritoneal cavity with the same result. If performed in time the operation will not entail opening the peritoneal cavity, the bleeding vessel may be found and ligatured after clearing the area of blood and clot, or, if it is not found, the bleeding can be controlled by packing the space between the rectus muscle and the posterior sheath. If necessary, the deep epigastric artery itself, which can be found on the deep surface of the rectus muscle about the level of the semilunar fold of Douglas, can be tied. It, or 1 of its branches, will be almost certainly the source of the bleeding. The experience of my 2 cases makes me strongly of the opinion that operative treatment is far more likely to avert a fatal issue than conservative measures, even granted the ease with which blood transfusions can nowadays be given.

The case record is published by courtesy of Dr. O. M. Holden, Medical Officer of Health, County Borough of Croydon, to whom my acknowledgements are due.

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Myasthenia Gravis and Pregnancy

BY

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THE association of myasthenia gravis and pregnancy has received very little attention in the English medical literature. Considerable research work has been published on myasthenia gravis but there are few recorded cases of pregnancy associated with it. This is no doubt due to the relative rarity of the disease. Indeed, Viets and his colleagues¹ report that of 63,268 admissions to the Boston Lying-in Hospital between 1900 and 1940, only 1 patient with myasthenia gravis was registered. Statistics from hospitals in Great Britain would probably substantiate this ratio.

A review of the literature indicates that since 1935, when prostigmin first became available for the treatment of the disease, the outlook has considerably changed. Where previously it was the practice to recommend termination of the pregnancy because of its adverse effect on the disease, there is no doubt that the consensus of modern opinion is entirely against this procedure. At the end of the nineteenth century Sinkler,² Punton,³ Burr and McCarthy⁴ reported cases in which an increase in severity developed during the first 3 months of pregnancy. It was probably not realized sufficiently at that time that the course of myasthenia gravis is characterized by periods of relapse and remission. There is no doubt, however, that pregnancy often

does cause profound changes in patients suffering from this disease, and this is probably the reason for the therapeutic abortions which were reported in the early literature. But it is true to say that of the more modern records some period of remission has occurred, either during the later part of the pregnancy or occasionally throughout the 9 months. Von Hösslin⁵ concluded that pregnancy had an unfavourable effect on patients and not only was this so during pregnancy but also in labour and the puerperium. He was so impressed that he advised patients who had myasthenia gravis not to become pregnant. In this he was supported by Warrington⁶ and Gemmell.⁷ Wolff⁸ also observed a relapse which began after the 1st pregnancy and became more severe during the 2nd, until it was terminated at the 4th month. Laurent⁹ described detailed observations on the effect of repeated pregnancies in a patient. He did not observe any change in the 1st pregnancy but relapse occurred in each of the 5 succeeding pregnancies, 4 of which were terminated by the 6th month. Of 7 patients who had 12 pregnancies, Kennedy and Moersch¹⁰ reported that in 5 pregnancies there was aggravation of symptoms during pregnancy and 4 of the patients improved following termination of the pregnancy or weaning of the child.

Throughout the remaining 7 pregnancies a change in symptoms was not observed. Silverstein¹¹ reported some improvement in his patient during pregnancy, while Milhorat¹² observed a remission during pregnancy and then a return of symptoms following abortion.

Since the introduction of prostigmin in the treatment of myasthenia gravis in 1935, it has been possible to assess more accurately the question of remission and relapse during pregnancy according to the amount of prostigmin required for satisfactory maintenance.

Tabachnick,¹³ who reported the onset of myasthenia gravis in a patient after her 4th pregnancy, observed a relapse during the first 4 months of her 5th pregnancy, but no definite remission during the last 5 months. He noted, however, that her daily requirements of prostigmin were considerably less during the first 4 months of the puerperium. In a series of well documented cases Viets, Schwab and Brazier¹ did not observe any relapse in 4 out of 8 cases during pregnancy and in the other 4 the relapses which occurred were mild, caused no anxiety and occurred mainly in the 3rd to the 6th month. These workers were impressed by the onset and completeness of the remissions, which they described as resembling "the sense of complete well-being experienced after an injection of prostigmin methyl sulphate, as used in the prostigmin test, only prolonged over days and months." These remissions were observed chiefly in the last 2 trimesters. In reviewing the effect of therapeutic abortion, Viets and his colleagues draw attention to the cases reported in the literature, in which the abortion was carried out at the end of the 1st or in the early part of the 2nd trimester and conclude that, if prostigmin therapy had been available, many, if not all, of these abortions could have been avoided.

LABOUR.

Doubtless because the physiological disturbances in myasthenia gravis were not fully appreciated and because it was erroneously considered that the uterus would fatigue, few patients who became pregnant were allowed to go to term. If they did, they were not allowed to deliver by the normal channels. Thus Gemmell¹⁴ delivered his patient by Caesarean section to avoid exhausting her. Of the few reported cases that have been delivered normally, the rapidity of the labour and the absence of complications have been especially noted (Tilney,¹⁴ Laurent,⁹ Viets, Schwab and Brazier,¹ Wilson and Stoner¹⁵). It is probable that the rapidity of the labour is due to the relatively greater relaxation of the voluntary muscles in these patients. In 1 patient observed by Viets and colleagues extra prostigmin was not required throughout the course of the confinement.

PUERPERIUM.

There is no definite agreement as to the effect of the puerperium on myasthenia gravis. Though Renter¹⁶ noted after delivery a relapse which terminated fatally, and Laurent⁹ a relapse which began 8 days after confinement; on the other hand Goldflam¹⁷ observed in his patient a period of well-being that lasted for 3 months after delivery in each of her 3 pregnancies. Viets and his colleagues¹ found that the remission experienced during the latter half of the pregnancy continued until 3 to 5 months after delivery. They did not observe any abrupt change after delivery in any case and regarded the return of increasing symptoms as the termination of the remission experienced during pregnancy. There is no evidence to support the contention of Stevens¹⁸ that the puerperium is an etiological factor in the onset of the disease.

THE EFFECT OF PREGNANCY ON MYASTHENIA GRAVIS.

Although on many occasions the relation of the endocrine glands to the causation of myasthenia gravis has been emphasized, no definite facts have yet been produced which would indicate the exact influence of any hormone on the disease. There is no doubt that female patients often have an increase in symptoms just before the onset of menstruation. There are several reports in the literature in which myasthenia gravis was first observed during pregnancy (Tilney,¹⁴ Grosse,¹⁹ Wolff⁸), yet it is difficult to see how pregnancy could be an important aetiological factor. Considering the large number of pregnancies which occur from year to year, and the relative rarity of the disease, one would expect, if pregnancy were an important factor, a much higher incidence of myasthenia gravis in women. Besides this, many patients who have had several pregnancies have not shown any evidence of the disease until the 3rd or 4th pregnancy (Kohn,²⁰ Freiberg,²¹ Reuter¹⁶).

There is no evidence that pregnancy precipitates the development of the disease, nor is there, as yet, any proof that the course of the disease is prejudiced as a result of pregnancy and labour.

THE CHILD.

The question of myasthenia gravis being a hereditary disease has been raised from time to time. There is only one recorded case of a myasthenic infant being born of a myasthenic mother. In this case Wilson and Stoner¹⁵ reported the delivery of a male child with the characteristic signs and symptoms of myasthenic gravis. After careful nursing his condition improved and at 5 weeks any evidence of the disease was not apparent. They were unable to detect any evidence of the disease in the 3rd year and assumed that the child was able to

eliminate the factor involved once he led a separate existence, though a period of 2 or 3 weeks was necessary for this purpose.

On the other hand 2 cases have been reported of myasthenia gravis in infants of 21 months and 23 months, both of whose parents were normal and in whose family there was no evidence of myasthenia gravis (Kawaichi and Ito,²² Booth²³). Although there are a few instances quoted in the literature in which therapeutic abortion was performed because of the fear of transmitting the disease to the child, considering the number of normal infants born of myasthenic mothers there is very slender evidence at present that the disease may be transmitted to the child.

CASE RECORD.

Mrs V. T., housewife, aged 28 years, was first seen in July 1942, complaining of tiredness, difficulty in chewing and swallowing and diplopia and drooping of the right eyelid. She had joined the Auxiliary Territorial Service 18 months before. A year ago she began to have diplopia which occurred at varying times but was most often present in the morning. Two months after this she had difficulty in chewing and swallowing and also noticed that she was unable to whistle and smile properly. Her voice became weak and faint when she had been talking for some time. Five months later her right eyelid began to droop. She felt tired and had attacks of nuchal pain which was more marked towards the end of the afternoon. She was married in July 1942, and 2 weeks later consulted her Regimental Medical Officer because of the aggravation of her symptoms. Her work in the A.T.S. did not affect her health and she had no weakness of the arms or legs.

Her previous medical and family history did not contain any significant features. She was discharged from the A.T.S. and was satisfactorily maintained with prostigmin 15 mg. 3 times a day and ephedrine ½ gr. twice a day. She was able to do all her own housework.

In November 1943 she became pregnant, and at the beginning of the 2nd trimester she found that to relieve her symptoms adequately she had to take

60 mg. of prostigmin daily, with the usual dose of ephedrine. She continued on this dose of prostigmin until the end of the pregnancy. In the last trimester she complained of sleeplessness, which was attributed to the effect of the ephedrine, and this was successfully counteracted by 1 gr. of secobarbital at night.

She was admitted to the Jeppia Hospital for Women on August 17th, 1944, and labour commenced spontaneously on the 20th. The 1st and 2nd stages lasted 11 hours and a live female child was delivered normally. The usual dose of prostigmin was given during labour but at the commencement of the 2nd stage prostigmin 2 mg. and atropine 1/200 gr. were given subcutaneously. The uterus contracted well in the 3rd stage and the placenta and membranes separated and were expressed without difficulty. The uterus maintained extremely good tone and no oxytocic drug was required.

During the first 4 days of the puerperium the daily dose of prostigmin was increased to 90 mg. and on the 5th day reduced to 60 mg., ephedrine gr. 1 being continued throughout. On the 9th day the daily dose of prostigmin was reduced to 30 mg. which effectively controlled her signs and symptoms. She was discharged on the 15th day. For a period of 9 months after delivery her chief complaints were ptosis, variable diplopia, aphonia and occasional dysphagia. This was adequately relieved by taking prostigmin, 15 mg., and ephedrine, 1/2 gr. twice daily. She volunteered the information that she felt better than before her pregnancy. When last seen in June 1945, that is, 10 months after delivery, she stated that occasionally her voice became fainter but that she had fewer attacks of diplopia and only her left eyelid drooped. She found it necessary, however, to take daily 3 tablets of prostigmin, i.e., 45 mg., with 1 gr. of ephedrine, to control her symptoms.

DISCUSSION.

In the present case an opportunity was taken to observe closely the effects of a 1st pregnancy on a patient who had been suffering from myasthenia gravis for 18 months. Before the pregnancy there had not been any significant variation in her signs and symptoms. The value of the observation was enhanced by the additional

objective evidence provided by the varying amounts of prostigmin required to control the signs and symptoms of the disease. Throughout the first trimester her condition was unchanged. About the end of the 4th month there was a mild relapse which continued until term and was adequately controlled by a slight increase in the daily maintenance dose of prostigmin. At no time was there any anxiety regarding her condition and the question of terminating the pregnancy was never raised. This, on the whole, is in agreement with the experience of Viets and his co-workers¹ in 2 of their patients. The labour of 11 hours was uneventful, delivery was spontaneous and, though some fibrillary twitching of her limb muscles was observed during labour, this was attributed to the extra dose of prostigmin which had been administered at the beginning of the 2nd stage. Throughout labour there was no evidence of any exhaustion of the voluntary musculature and at no time was there any indication of inertia or fatigue of the uterine muscles. It is to be noted that the work done by the involuntary muscles of the uterus had not the effect of increasing the signs and symptoms of skeletal muscle weakness.

Although some records describe relapse in the puerperium this was not the experience of Viets and his co-workers.¹ In the present case the transient mild relapse occurred during the first 5 days of the postpartum period, and necessitated a slight increase in the maintenance dose of prostigmin. At no time were there any severe manifestations and by the 5th day of the puerperium the patient's condition was the same as that obtaining in the latter half of the pregnancy.

A definite remission became manifest on the 9th day of the puerperium and continued for 9 months after delivery. The remission was abrupt and definite and the control of the symptoms was maintained

by less prostigmin than was required before her pregnancy. At the time of writing she is now adequately maintained on her pre-pregnancy dose of prostigmin.

The child was normal and was nursed without difficulty for 7 months. In growth and development the baby pursued an uninterrupted course and at no time did it display any evidence of myasthenia gravis.

CONCLUSIONS.

1. The literature on myasthenia gravis associated with pregnancy is reviewed.

2. A case of pregnancy in a patient with myasthenia gravis is described in which the chief features observed were a mild relapse in the latter half of the pregnancy and the first 4 days of the puerperium. The labour was normal and a normal child was delivered. A definite remission of signs and symptoms was observed on the 9th day of the puerperium which continued for 9 months.

3. There is no indication that pregnancy, labour or nursing adversely affects the course of myasthenia gravis in a patient treated with prostigmin and ephedrine.

We wish to express our thanks to Mr. Glyn Davies for clinical facilities and access to the patient who was under his care. The expenses of the work were partially defrayed by a grant from the Medical Research Council to one of us (A.W.).

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Notes on the Treatment of Vesicovaginal Fistula

BY

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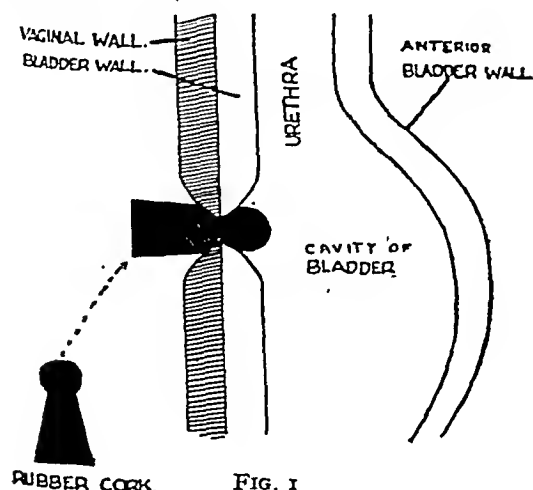
Late Honorary Senior Surgeon, Samaritan Hospital for Women, Belfast.

Infection of the Bladder and Vagina.

To operate on a recently developed fistula, when the tissues are oedematous is to court failure. At least 3 months should elapse from the date of onset to achieve success.

The patient will then require some days of preparation, as the vaginal wall has usually become unhealthy and somewhat sodden from leaking urine.

If there is an infection of the bladder it should be eliminated. To achieve this I conceived the idea of corking the fistula for a few days before attempting to operate; washing out the bladder daily with sterile water; and changing the urinary reaction. By this means, also, the vaginal walls are kept dry, and with daily douches soon regain a more normal condition. For the purpose of "corking" the fistula I use rubber corks of various sizes, filing a neck at the small end in the shape of a stud (Fig. 1).



This cork does not, in any way, injure the edge of the fistula or cause inconvenience to the patient and she need not be confined to bed. It is necessary to impress on the patient the fact that this is only the first stage of the operation as, when she finds that there is no more urine leaking into the vagina, she may imagine that she is cured and ask to be allowed to leave the hospital.

Prolapse of the Mucous Membrane of the bladder into the fistula while it is being stitched may prevent the perfect coaptation of the muscular layer of the bladder thereby causing a leak. To overcome this difficulty I devised the following procedure, which made more certain a perfect operative result. Following the separation of the walls of the vagina and bladder as in a colporrhaphy, I adopt in reverse the method of treating the stump of the vermiform appendix, where, after inserting into the caecum a purse string suture around the appendix stump one pushes the stump into the caecum.

I insert a purse-string suture of fine catgut, as near the refreshed edge of the fistula as possible, leaving it untied and the suture long. Then, passing a sound through the urethra into the bladder and out at the fistula, the free ends of the suture are tied behind the bulbous end of the sound (Figs. 2a and b). On withdrawing the sound, the free ends of the suture now come out at the urethra (Fig. 3). By gentle traction on these ends the edges of the fistula are infolded into the bladder and out of the way, so allowing interrupted stitches to pass

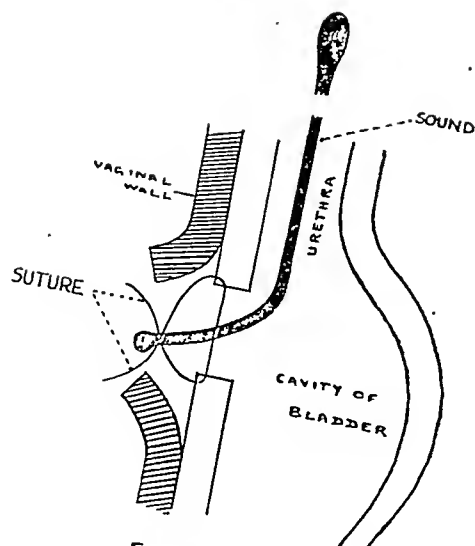


FIG. 2 a.

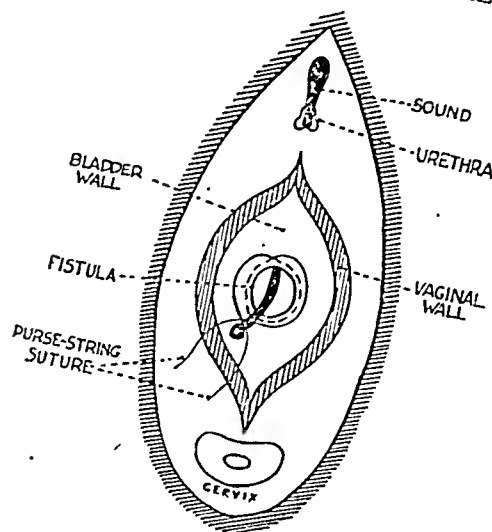


FIG. 2 b

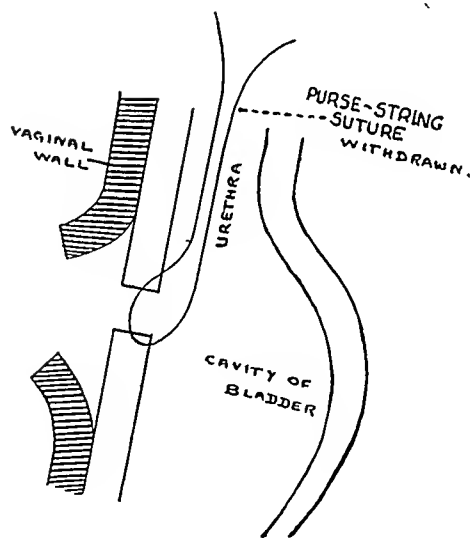


FIG. 3

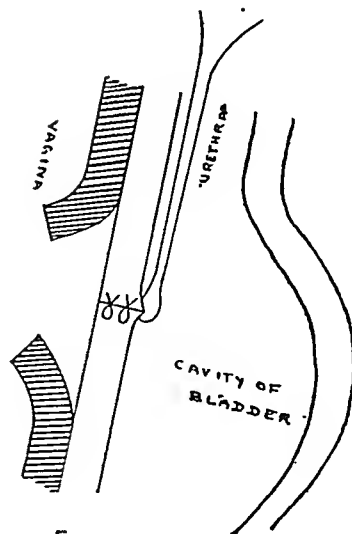


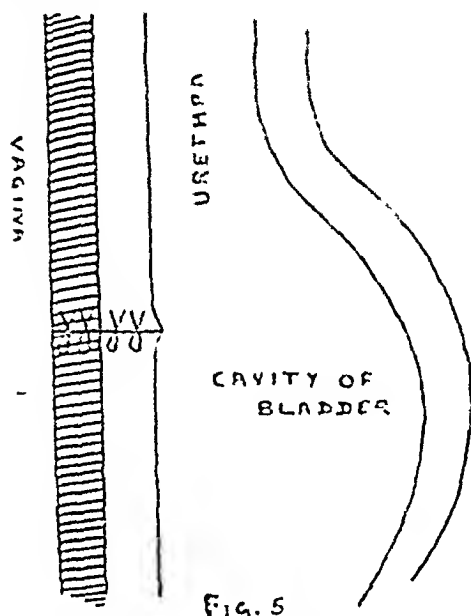
FIG. 4

through the bladder musculature down to, but not through, the mucosa without risking prolapse of the mucous tag, thus accomplishing perfect sealing (Fig. 4). The purse-string suture is then removed *via* the urethra. The vagina wall can then be dealt with as in a colporrhaphy (Fig. 5).

Removal of Blood Clot from the Seat of Operation.

In all operations for vaginal repair the presence of blood clot, no matter how small the amount, at least retards, if it does not entirely prevent perfect union. The use of swabs has not only the dis-

advantage of wasting time and disturbing the continuity of the operation, but also the act of swabbing is bound to injure the tissues, even to a slight degree, which is detrimental to a good result.



I have, therefore, for a long time given up their use in all vaginal operations and work entirely under running sterile water. The douche stand is placed in such a position that the nurse, detailed especially for the purpose, and standing beside me, can keep up continuous irrigation over the

seat of operation. A good nurse soon learns to regulate the strength of flow to suit the stage of the operation, thereby becoming an important member of the surgical team. There is no doubt that the healing process following under water operation is quicker and better; the patient also has a much more comfortable convalescence.

After Treatment.

It is not necessary to subject the patient to the discomfort of self retaining catheters, or to vaginal packing.

If the patient is nursed on her back for 3 or 4 days and catheterized with a soft rubber catheter every 4 hours for the first 48 hours, and then every 6 hours for the following 4 days, she can then micturate normally without any fear of doing harm to the newly healed tissues. If, however, the act is found impossible, as so often happens in repair operations catheterization night and morning will be found sufficient, until the patient is allowed up on the 14th day, when there will be no difficulty.

Vaginal Packing.

This is unnecessary, in fact, like swabbing it may endanger the vaginal stitches, and if they give way the bladder loses its chief support.

Lawson Tait*

BY

LEONARD GAMGEE, Ch.M., F.R.C.S.

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TO-DAY we celebrate the hundredth anniversary of the birth of Lawson Tait—a great surgeon and a great personality. Tait was the son of Archibald Campbell Tait, a writer to the signet, who practised in Edinburgh and who was a cousin of Archbishop Tait of Canterbury. Perhaps I should have said “reputed son,” for there is a doubt as to Tait’s parentage. Tait was born on May 1st, 1845, in Edinburgh, and was educated at Heriot’s Hospital, one of the great schools which have contributed so much to Scottish education. Tait underwent his medical education in Edinburgh, and there he came in close contact with James Syme and J. Y. Simpson, for both of whom, as men and surgeons, he had great admiration. He obtained the conjoint qualification of the two Royal Colleges of Edinburgh in 1866, and in 1867 was appointed House Surgeon to Wakefield Infirmary. It was in Wakefield that he met the lady whom he married, his marriage taking place in 1871. While at Wakefield Tait performed ovariectomy 5 times. Things must have been different then from what they are now, for it is difficult at the present day to imagine a house surgeon performing abdominal operations which his chiefs would shrink from doing. That he did this is proof of that courage which was one of the outstanding features of Tait’s surgical career

for, to quote his words, “The results of ovariectomy I have seen in Edinburgh were truly awful—some 30 cases and not a recovery.”

That at that time Tait’s interest was not only in the surgery of the abdomen is proved by the fact that in 1870 he wrote a pamphlet—he loved writing pamphlets—on the treatment of cleft palate. His method of treatment is described with that clarity which characterized all his surgical writings, and his methods anticipated in important particulars the work of Arbuthnot Lane in our time. Tait wrote on cleft palate 75 years ago, and he did not leave much unsaid. There is the same “complete” note about Tait’s description of cleft palate and its treatment as there is in Brodie’s description of chronic bone abscess and in William Hey’s description of injury to the internal semilunar cartilage of the knee.

Tait came to Birmingham in 1870, purchasing the practice of Dr. Partridge in Lozells Road, and there he settled down as a general practitioner. Soon after coming to Birmingham, finding it necessary to add to the income derived from his practice, he became a leader writer on the *Morning News*, a daily paper which had not a long life, but which had the distinction of being edited by George Dawson, a Nonconformist minister, very famous in his day, a man of marked individuality and in whom there was a certain spark of genius.

The practice in Lozells Road did not give scope for Tait’s tremendous energy and

* The Tait Oration, delivered on the occasion of the Lawson Tait Centenary Celebration at the Queen Elizabeth Hospital, Birmingham, on June 29th, 1945.

transcending ability, so he took the diploma of Fellow, first of the Royal College of Surgeons of Edinburgh and then of the Royal College of Surgeons of England, and he gave up general practice and started practice as a consulting surgeon. This he did at the age of 26 and without holding a hospital appointment. Courageous as ever! It goes without saying that he realized the necessity of being on the staff of a hospital and so, at his instigation and with the help of Arthur Chamberlain, the Birmingham Women's Hospital was founded. At first this hospital was at No. 8 The Crescent, but was afterwards moved to some old premises at Sparkhill. I have myself heard Tait say that the greater part of his work was done in a converted farmhouse, and this was the truth. I shall have more to say about his views as to hospitals and their construction rather later. With his membership of the staff of the Women's Hospital Tait's phenomenal surgical career began, a career which is the story of a remarkable sequence of advances in abdominal surgery, which laid the foundations of many surgical procedures which we now look upon as quite ordinary. It is now for me, as the mouthpiece of the hour, to dwell on these achievements of Tait's and to attempt to draw a picture of what surgery owes to him, and of his striking personality.

At the time with which I am dealing the most spectacular and talked-of gynaecological operation was ovariectomy, and I have mentioned that Tait did this operation 5 times while he was house surgeon at Wakefield. Spencer Wells was at that time the man who had a great reputation as an ovariectomist, but his mortality-rate was nearly 30 per cent. Tait put down this high rate—and apparently rightly—to the fact that Wells treated the pedicle extra-peritoneally by the application of a clamp. Keith, of Edinburgh, lowered this high mortality-rate by cauterizing the pedicle

and dropping it back into the peritoneal cavity, but this was rather a laborious process for Keith kept searing the pedicle with his cautery for quite 10 minutes. Tait further reduced the mortality-rate by ligaturing the pedicle, this taking a tithe of the time that canterization took. Anything that saves time in surgery saves life. Tait brought down the mortality-rate for ovariectomy from Spencer Wells's 28 per cent to less than 4½ per cent—a great achievement for those days!

On February 2nd, 1872, Tait operated on a woman whom he had seen in consultation with Matthew Hallwright. The patient had, for a long time, suffered from abdominal and pelvic pain. Tait diagnosed chronic disease of the left ovary and advised laparotomy. This he did and found a left ovary the size of a pigeon's egg with a chronic abscess in its interior. He removed the ovary and the patient was cured. Tate was the first man to make such a diagnosis and to remove a diseased small ovary. His claim that he was the first man to do oöphorectomy raised a storm of controversy, the reason for this being that Trenholme of Montreal, and Hegar of Berlin, during the next 2 or 3 years recorded cases in which they had done this operation and that Tait had not published a record of his case until 11 years after he had operated. Those were days of bitter controversy in the surgical world and it was asserted that, as Tait did not put his case on record at the time, his statement that he did this operation in 1872 was untrue. Apart from Tait's assertion that he did this operation, it may be noted that he was helped at the operation by Bennett May, who confirmed Tait's assertion, and those who knew Bennett May as well as I did never doubted the truth of anything he said. Tait's position as the first surgeon to remove a diseased small ovary seems unassailable. That this operation has often been done

unnecessarily by Tait's imitators does not detract from his fame.

While talking of tumours and diseases of the ovary, it may be recalled that in 1937 Meigs and Cass, two American gynaecologists, described a condition in which a non-malignant fibroma of the ovary may be associated with ascites and hydro-thorax, and called attention to the fact that removal of the ovarian tumour is curative and that the fluid does not re-accumulate. The condition is now known as Meigs's syndrome. It should not be so called, for Tait described the condition in 1891, and related how in such a case he had removed the tumour and the fluid did not re-accumulate. Thus, he anticipated Meigs and Cass by 46 years, so really we should speak of Tait's, not Meigs's, syndrome.

Perhaps one of the most dramatic first operations ever performed was done by Tait in 1883, when he operated for ruptured tubal pregnancy. This is a matter worth dwelling on for a few moments. I think it was some time in 1882 that he saw, in consultation with the same Matthew Hallwright, a woman dying from intra-peritoneal haemorrhage, which Tait diagnosed was due to ruptured tubal pregnancy. Hallwright urged operation. This operation had never been done and Tait was appalled at the prospect of doing it, and did not operate. However, he was a big enough man to consider any suggestion and soon afterwards he saw a similar case with Dr. Spackman of Wolverhampton. He operated and the patient died. Then he saw a case of the same kind with Edward Sutton Page of Solihull. He operated and the patient recovered. Tait, by his courage and skill, had shown how women's lives could be saved when suffering from the effects of a previously considered fatal surgical catastrophe. How simple it all seems now. How clear to us that operation is the only treatment in such cases and that the

operation is by no means a difficult one, but it is not in surgery only that it requires the great man to make the simple discovery. If Tait had done nothing else that was notable, his name would go down to posterity for this. Not even his many opponents can deny that he did this operation in 1883, and that he was the first man to operate for ruptured tubal pregnancy.

Perhaps not so spectacular as this, but equally important, possibly more important because the condition is more common, was Tait's work on inflammatory diseases of the uterine appendages. He was the man who insisted that many women were suffering from abdominal pain and ill-health owing to their having inflammation of the uterine appendages, often following gonorrheal infection. In 1877 he opened the abdomen of such a patient and found a pear-shaped swelling attached to the left corner of the uterus. He tapped this with a trochar and withdrew altered blood. He did not remove the swelling, but drained the cavity, diagnosing that the condition he was dealing with was really due to inflammation of the uterine appendages. He went on investigating such cases and a few months afterwards he removed his first pyosalpinx. Hegar had removed a pyosalpinx a few months before Tait did; so had Spencer Wells. Be that as it may, it was Tait who pointed out the frequency of inflammation of the appendages, it was Tait who insisted on operation in such cases, and it was Tait who met with fierce opposition and virulent abuse for this insistence. In this country and America, operation for removal of diseased uterine appendages has come to be known as Tait's operation. It was Tait's senior confrères, men like Spencer Wells, Matthews Duncan and John Williams, who opposed the performance of this operation, and they it was who, with the *Lancet* (August 21st, 1886) thought they could successfully dis-

parage the operation by referring to it as "spaying." In a letter to the *Lancet* Tait dealt with this name for his operation, and he did so in his usual direct and unblatant language. No man could speak more plainly, when occasion required. Gradually his more enlightened confederates, as for instance Greig Smith of Bristol and Cullingworth of Manchester, came to support Tait. None admitted more fully than Tait did that the *ardor operandi* of many of his less experienced followers led them to remove the appendages in patients in whom it was not in the least necessary to do so, but Tait cannot be blamed for that.

Tait was furiously attacked for his views on the pathology and treatment of inflammatory diseases of the appendages. Why was he so fiercely attacked by men of the standing of Spencer Wells and Matthews Duncan? I cannot help thinking that a chief cause of their attacking him was jealousy, that jealousy of which quite an able plodder is so often guilty when he is up against a genius. Another cause of jealousy was, it seems to me, that Tait was a provincial surgeon living in the outer darkness of Birmingham. He himself gloried in this and never seemed inclined to move his headquarters to London. Patients came to Birmingham to consult him from all over the world—and that was enough for him. As an illustration of Tait's pride in being provincial, perhaps I may be allowed to quote from his account of his American tour in 1884, in which he says that on the library table in the medical school of Harvard University he found "a well-used copy of Mr. Sampson Gamgee's book on Fractures—a fragment of comfort for my provincial soul." Another cause of the attacks on Tait was without doubt his personal characteristics. He was always sure of himself. He knew what a big man he was and that he stood head and shoulders above his attackers. What is more,

he did not hesitate to say that he knew this. If he thought a man was a fool, he told him so. This does not make for friendly controversy, more especially when one of the controversialists glories in a fight. These attacks did not disturb Tait. He could be trusted to give more punishment than he took. Tait's work on inflammation of the Uterine Appendages will, I think, always be looked upon as his *magnum opus*.

In 1879 Tait operated on a patient with an enlarged gall bladder, removing a gall-stone and draining the gall bladder, the patient recovering. He thought, and it was generally thought in this country, that he was the first to do this operation, but it appeared that cholecystotomy was done in 1867 by Blobbs, who was Professor of Surgery in the University of Indiana, U.S.A. However, Tait was the first man in Europe to do it, and he must be looked upon as the pioneer of gall-bladder surgery.

During the early part of Tait's surgical career Lister's system of antiseptic surgery was in course of evolution, supported by most surgeons, vehemently opposed by others, as for instance Savory, perhaps most vehemently of all by Tait, who claimed that he obtained as good results regarding wound treatment as did the Listerians with their tremendous attention to detail and the frequent dressing of their wounds. Tait would not let any chemical get near his wounds. He cleaned his instruments by pouring boiling water over them, and after a time he had the water with which he washed out the peritoneal cavity boiled. He was very fond—too fond to my way of thinking—of washing out the peritoneal cavity. I have heard him say that for this purpose he used Birmingham tap water, which, he said, contained "thirty-different kinds of beasts." The fact is that Tait would not admit that sepsis of a wound is caused by organisms. Consequently he did not realize that boiling the water used for washing out

acted by killing the "thirty different kinds of beasts." He dressed his wounds with a pad of dry absorbent cotton wool tissue, and he dressed them very infrequently. It does not detract from Lister's great work to say that Tait was, without doubt, the great inaugurator of aseptic, as opposed to antiseptic, surgery, and it is the methods used by Tait that we all now follow. Tait entirely failed to see that regarding wound treatment he and Lister were working along parallel paths. No, he even said, in a pamphlet published in 1883, "I have already seen enough of the so-called antiseptic system of Lister to be able to say that it has been finally dismissed from the Department of Surgery as having done far more harm than good. I venture to predict a similar fate will meet it everywhere else, and I take to myself some credit for having burst one of the largest, best-blown bubbles ever displayed to a surgical audience."

Tait was a great advocate of the small hospital and, as I have said, he did his hospital work in a converted farmhouse. In 1877 he wrote a letter, which created a great sensation, to the Governors of the General Hospital, pointing out the high post-operative mortality, more especially in cases of primary amputation, and put down as the cause of this the presence of so many surgical patients in one building. He urged that the Governors should sell the site of the hospital and build four or five small hospitals just outside the centre of the town. I suggest that Tait's view was mistaken, for he attributed the bad results to the building, not to the men working in it. To illustrate this point, I may say that I myself entered as a student in 1886, 9 years after Tait wrote his letter, and I vividly remember the surgeon for whom I did my dressing operating in an overcoat bespattered with patches of dried blood and pus. I well remember that one evening I was standing in the theatre of the old

General Hospital watching one of the surgeons operate on a case of strangulated femoral hernia. I had my hands in my pockets. The surgeon had opened the hernial sac, when he asked me if I had ever felt the edge of Gimbernat's ligament. I answered that I had not, and he said: "Feel it now." How well I remember taking my hand out of my pocket and passing a finger into the hernial sac. I grant that the General Hospital Building in Summer Lane was out of date, but surely Tait was mistaken in the main contention in his letter to the Governors. He should have laid down the bad post-operative results, not to the building, but to the men working in it. Tait was on safer grounds when he asserted that hospital buildings should be lightly constructed, preferably on the pavilion system, and that at the end of 30 years or so they should be pulled down and other, similar but improved, buildings erected. He was very insistent on this point.

His membership of the teaching staff of the medical school was short. He was appointed Professor of Gynaecology in 1888 and retired in 1893. I had the privilege of attending his lectures, and my recollection of them is that they were above me—they might easily be that—and that they presumed an amount of knowledge that we students did not possess. Recalling his lectures, I think that they were admirable for the postgraduate; not so admirable for the student.

Tait performed a great service to the profession in 1888. The Medical Defence Union had been started in London in 1885, but was a failure. In 1888 it was re-founded in Birmingham with Tait as a very active President, and as a result of his energy the Union at once began to flourish. He gave up the Presidency in 1893, because the profession was angered at the way he spoke of vivisection and its advocates at a

meeting of the Church Congress. He was an ardent, and somewhat irrational, opponent of vivisection. However, he had set the Union on the road to success.

As I have said, Tait was satisfied to retain his consulting room and nursing home at No. 7, The Crescent, and it is not going too far to say that, while he was at the height of his fame, No. 7, The Crescent, Birmingham, was one of the most famous spots in the surgical world. Men came from America and most European countries to see Tait's work; such was his fame.

Tait's interests were not purely medical. In 1886 he was a candidate for Parliament, fighting the Bordesley Division of Birmingham as a Gladstonian Liberal, but he was unsuccessful. He was for some years a member of the Birmingham Town Council, doing most of his work on the Health Committee and writing various pamphlets on refuse-disposal, housing etc.

Tait matured early. We have seen that he did abdominal operations when he was 24 years old. His great original work was finished by 1890, when he was 45. He went on practising and writing, but his work after 1890 was not epoch marking, as it previously had been. He died in 1899, when he was 54.

In appearance Tait was striking: he was short, massively built, with a large head. He was a man who would be noticed anywhere. He used to drive about Birmingham in a victoria drawn by a pair of dapple greys, and it is said that he always had four pairs of these horses. He used to wear a soft wideawake hat and a short jacket, usually of velvet. He insisted on Christopher Martin, then his assistant, wearing a tall hat and frock coat. Martin asked him why he did so and why he would not let him wear a soft hat and short jacket. "Because" Tait answered "you are only Christopher Martin but I am Lawson Tait." A stranger seeing Tait in his car-

riage could not fail to ask "Who is that?" Tait had a beautifully modulated voice and a very sweet smile, but he could, and often did, burst out suddenly into a furious rage. It is said that on one occasion—it was in the early days of the telephone—he kept getting wrong numbers or something of that kind, and he broke out into one of his tempers. He seized the telephone apparatus, tore it from the wall, threw it to the floor and literally danced on it, smashing it to pieces. Doubtless he felt much better after doing this. He could, when irritated, show a pretty sarcasm. As an example I will quote a story which I have myself heard him tell. He had been called into the South of England and had operated on the wife of a very rich man, who asked Tait his fee. Tait named a large one, "too large" the husband said. Tait answered: "Well, on one page of my fee book I put the name of the payer and the sum paid. On the opposite page I put the names of defaulters. I do not care which page your name appears on, but it is going to appear on one of them." I need hardly say that Tate received his fee.

Tait was a peculiar man of uncertain moods. He told me that he had once been called to Liverpool and had received a large fee, the whole of which he spent on carved ivory figures before entraining for Birmingham. He was a collector of these and other curios, but not a very discriminating collector, and I am afraid had many shams passed off on him. He was fond of entertaining, more especially of giving large dinner parties. Sometimes these dinners were fit for a king; sometimes, well not quite so good. With all his occasional bad tempers, with all his high estimation of himself, Tait was at heart a very kind man. He took many patients into his nursing home and operated on them without charging a fee. I must ask forgiveness if I strike a personal note. Tait and my father were enemies and

never spoke to each other. Why, I do not know. Yet, when first I became a member of the staff of the General Hospital and started in practice, Tait was a great friend to me. He was too big a man to bear a grudge and to remember old enmities.

Tait, as I have said, had many enemies, some of whom attacked him fairly, others unfairly, the chief mode of attack of the latter being to assert that his statements as to his work were untrue. As regards his *magnus opus*, i.e. his investigation of and his operation for inflammation of the uterine appendages, Tait admitted that pathologists had for a long time described the condition, but then apparently came a full stop, for the clinicians before Tait's time failed to recognize these cases and had failed in their treatment of the patient. At the International Medical Congress in 1881 Spencer Wells came out with his famous piece of criticism regarding these cases: "It is very extraordinary that so many such cases should occur. I have seen only one in my lifetime. Perhaps they all go to Birmingham." Surely we know now that Tait was speaking the truth: present-day experience proves that. No, it was not that Tait was untruthful, but that his accusers did not appreciate the clinical symptoms and signs shown in these cases: while treating these women, who were often reduced to chronic invalidism, they played about with pessaries and douches, while Tait, who made an accurate diagnosis, removed the appendages and cured his patients. The question arises: were these older gynaecologists clinically ignorant or were they all-knowing and Tait untruthful? There can, I suggest, be only one answer. Tait was speaking the truth and was working on the right track. But these battles are of the past and we of our time all recognize Tait's work in this sphere of surgery.

Tait was a great clinician. In questioning and examining a patient he was quick and aimed straight at the centre of the problem, brushing aside the extraneous. He had clinical intuition developed to a remarkable degree. I have seen him operate: he made a small incision through which he introduced two fingers, and by touch alone he made out the condition with which he had to deal. He was a marvel at separating adhesions. I have heard him say that he gained this skill by practising peeling oranges. He was a very quick operator. I once saw him open an abdomen, remove two ovarian cysts to which coils of intestine were densely adherent, and the patient was back in bed 20 minutes after the incision was made. While he operated there was absolute silence. Watching him operate made one think that it was all so easy, surely a supreme proof that the operator is a master. It is interesting to recall that he never operated in an operating theatre, but always in the patient's bedroom, the patient lying on a simple wooden trestle table.

Tait was the Napoleon of surgery—clear thinking, courageous, original, inventive, not bound by any precedent. He was a man of many facets, and that he was a surgical genius there is no doubt. With the modern developments of abdominal surgery there is a tendency to forget the man who, by the brightness of the lamp he lighted, showed the way. He dispersed once and for all the fear and trepidation with which surgeons before his day opened the peritoneal cavity. He simplified abdominal surgery. He was one of the greatest surgical originators and pioneers of modern times. Birmingham must always be proud that Tait was one of her citizens and that it was here that he did his wonderful work.

BOOK REVIEWS

"Midwifery for Nurses" (Thirteenth edition). By HENRY JILLET, B.A., M.D., F.R.C.P.I. Consulting Gynaecologist, Rotunda Hospital Dublin; late Consulting Obstetrician to the Department of Health, New Zealand, etc. 1945. 456 pages. London: J. & A. Churchill, Ltd. Price 12s. 6d.

THIS is intended to be a textbook for the pupil-midwife. As such there is a fairly well defined range of subjects which must be covered, and this is done. The subject matter is clearly set out as would be expected of so eminent an author and teacher. Emphasis is rightly laid on the normal, which will constitute so large a portion of the midwife's work. Methods of examination are well described, and the importance of abdominal examination is stressed. The description of the physiology and management of normal labour leaves little to be desired, while there is an excellent chapter on asepsis in midwifery. The preparations to be made for the conduct of labour are clearly detailed. Not only will the midwife in training find this of value, but even established and experienced midwives could study this chapter with profit.

It is surprising to read, however, that "obstetrical anaesthesia" induced by a well-trained nurse using chloroform or ether is considered permissible. The Royal College of Obstetricians and Gynaecologists condemned their use in its carefully considered report on the subject. Recent correspondence in the medical press has shown quite clearly that great improvement is still necessary in the administration by midwives of gas and air for analgesic purposes. Lack of understanding of the principles of analgesia, lack of interest or want of ability, among practising midwives, to maintain in order simple apparatus has been demonstrated. It would seem that the College was correct in

advising against the use, by midwives, of these poisonous substances.

Abnormal presentations are so presented that the pupil-midwife can form a clear mental picture of what is happening as the child is born or as labour comes to an *impasse*. But the description of antepartum haemorrhage is spoiled by the prominence given to the making of vaginal examinations, the rupturing of membranes and plugging of the vagina—all of which are contemplated as being done by the midwife if she cannot obtain medical aid. Nowadays the medical practitioner who makes vaginal examinations on cases of antepartum haemorrhage, before sending them into hospital, is criticised. Why tell the pupil-midwife to do something which no hospital is prepared to teach her to do, which she is most unlikely to do adequately, and for which even the skilled medical practitioner requires the administration of an anaesthetic? Has not the time come when this teaching should be revised?

It may be objected that these are matters of opinion. But conservatism in teaching may be persisted in to such a degree that the teaching becomes out of date. This is seen on the chapter dealing with puerperal sepsis. Here we find, laboured at length, a distinction between sapraemia and septic infection. An attempt is not made to explain that the mode of infection, the signs and symptoms, and responses to treatment may vary according to the organism responsible for the infection. The streptococcus is the streptococcus—no differentiation is made between haemolytic streptococci and anaerobic streptococci. Turning to treatment it is astonishing to read that "as a rule, the first step in the treatment is to obtain some of the discharge from the uterus for bacterial examination, as injections of a vaccine prepared from the same type of organism as that with which the patient is infected or of a serum

sometimes prove of great value and are usually tried" (reviewer's italics). It is equally astonishing to learn that "of the many different remedies which have been suggested for the cure of a general infection it is probable there is none so effective as good nursing." This is frankly untrue. Septicæmia due to the *staphylococcus aureus* was almost invariably fatal, irrespective of the quality of the nursing, prior to the introduction of penicillin. Penicillin is not even mentioned. This whole chapter largely requires to be rewritten.

The chapter on obstetric operations is poor even for a nurses' textbook. It may be Dr. Jellett's practise to induce labour by bougies or the stomach tube in cases of contracted pelvis, but others may doubt whether it is "the best method." Must the vertex present before the forceps can be applied with safety? Why not the face, or the after-coming head? Is Caesarean section really so unimportant to the nurse that it can be dismissed in $4\frac{1}{2}$ lines, while $7\frac{1}{2}$ are devoted to pubiotomy?

The section dealing with the normal and abnormal infant is adequate though sketchy in parts.

The book ends with a number of valuable appendices dealing with cancer of the uterus and breast, obstetrical outfits, prevention of sepsis, antenatal and postnatal exercises, and general information and recipes. The book is of suitable size, well bound, on good paper, well printed and illustrated. That this book has appeared regularly for 44 years is a tribute to its worth. It certainly deserves to be kept up to date. In spite of all its good qualities some portions of this latest edition still require much further revision.

ANTHONY W. PURDIE.

"A Textbook of Pathology of Labor, the Puerperium and the Newborn." By CHARLES O. McCORMICK, A.B., M.D., F.A.C.S. Clinical Professor of Obstetrics, Indiana University School of Medicine. 1944; 399 pages. London: Henry Kimpton. Price 37s. 6d.

THE scope of this book is limited to the consideration of labour, the puerperium and the new-born child. Pregnancy is excluded. It is based on the lectures given by the author over a period of 25 years to senior medical students of his own university.

The field covered is wide while not exhaustive. An attempt is made to set out the essentials of present-day obstetric thought, avoiding as far as possible controversial matter and theoretical discussion. Therefore neither in its scope nor in manner of its presentation can it be regarded as a complete obstetrical textbook for the medical student. Yet it is not a cram-book. It contains a great amount of factual matter, presented in a didactic manner, with unmistakable emphasis on important points. Throughout the text clarity and brevity are the dominating features. As far as is possible tabular presentation of material is used, sentences are often not completed while the second person is used in describing therapeutic procedures. There is efficiency but with haste. The liberties taken with the language would be deplored by the grammarian and by those to whom style in writing is still a matter of moment.

The subject matter is sound. There might have been a little amplification of the reasons for deciding on certain therapeutic measures, while a little less detail in description of some operative techniques would not have mattered. The student is not going to do Caesarean sections without further training and wider reading, but he may well have to look after a case of eclampsia. He would therefore be interested to know, in more detail, why Caesarean section is sometimes employed in eclampsia with a mortality of 30 per cent to 40 per cent, while conservative treatment may result in a mortality of not more than 10 per cent. But he will not be interested in the description of three different methods of performing extra-peritoneal Caesarean section. One might question the wisdom of yielding to the demand of husband and wife for sterilization at the first Caesarean section, done on a healthy woman for contracted pelvis. For all that the subject matter is sound and up-to-date.

The book is well printed, easy to read, beautifully and clearly illustrated—in fact the text is sometimes superfluous, so fine are the illustrations.

The student who uses this in conjunction with his clinical teaching may acquire a sound knowledge of the field covered. The practitioner may turn to it in a hurried moment and find a clear authoritative direction. The specialist will be less interested, but may glean some new ideas for the presentation of his subject. The book closes with

so obtrusive aphorism ("I learned from here and there") which all could read with interest and, perhaps, with profit.

ANTHONY W. PURDIE.

"Recent Advances in Obstetrics and Gynaecology." By ARTHUR W. BOWEN and LESLIE H. WILLIAMS. 6th edition, 1945. London: J. and A. Churchill.

It is a pleasure to welcome a new edition of this volume, which has for nearly 20 years presented all that is best in current work in the 2 subjects. Here is a volume packed full of factual information, including much that is truly recent, and which admirably achieves the aim of the authors, set out in the preface, to give not only lists of references to recent papers, but also to indicate and crystallize the general trend of thought along various lines.

The authors are fortunate in having again secured the collaboration of Mr. Wilfred Shaw, who contributes an excellent chapter on Ovarian Tumours, and helps to clarify a difficult subject. Dr. Rohan Williams has revised his chapters on Radiology in Obstetrics and on Radiological Investigation and Diagnosis in Gynaecology, and gives a particularly useful description of the methods of X-ray pelvimetry and of the classification of pelvic types. Dr. W. M. Levitt has contributed a full account of modern views on the Radiotherapy of Gynaecological Disorders.

This book contains much material which has appeared in earlier editions, and which is rightly regarded as authoritative. In addition there is much new material, summarizing advances over the past 20 years in such important subjects as Nutrition in Pregnancy, Vitamin K, Stillbirth and Neonatal Death and Erythroblastosis. The chapter on Erythroblastosis gives perhaps an over-simplified account of a matter which is becoming daily more complex. Little mention is made of the subgroups of the Rh factor or of incomplete antibodies, but these are minor omissions which will doubtless be remedied in future editions when more work has accumulated on this subject.

In a book which deals with so many matters of perennial and topical interest it is difficult to select any part for special mention. The chapter on Cancer of the Uterus is already well known as a comprehensive account of the relative merits of the

different forms of treatment available. A very full account is given of the investigation and treatment of sterility and the section on Leucorrhoea includes important original work on chronic cervicitis. The chapter on Sex Hormones summarizes recent knowledge on the chemistry, physiology and therapeutic applications of these substances.

This is a book, then, which is an invaluable addition to the library of all who are practising obstetrics and gynaecology and one which should prove particularly useful to those studying for higher examinations in these subjects. The authors are to be congratulated on this latest addition to the literature and on the excellent balance of views which is maintained throughout.

"Précis d'Obstétrique." By FABRE. Volume II. Abnormal Obstetrics. 8th edition. 1940. Paris: Librairie J. B. Ballière et Fils.

THE 8th edition of Fabre's "Précis d'Obstétrique" was published in 1940. It is 1 of a series of 48 volumes, designed for students working for the Doctorate of Medicine.

It is a little difficult to appraise a work produced over 5 years ago, but it must be admitted that there is a good deal in this volume which would not meet with the approval of most British obstetricians.

It is surprising to find the main alternatives for the treatment of placenta praevia before labour to be plugging the vagina or digital dilatation of the cervix, followed by bipolar version, while Caesarean section is reserved only for primipara where resistance of the cervix prevents the latter manoeuvre. De Ribes' bag—now largely out of favour in this country—receives considerable attention.

Mention is not made of the use of the Aschheim-Zondek and other pregnancy tests in the management of abortion or in the diagnosis and after treatment of hydatidiform mole.

The section on pregnancy toxæmias is confused. Mention is not made of the role of vitamin B in hyperemesis. Albuminuria and eclampsia are dealt with as entirely separate and disconnected conditions, and in neither section is any reference made to the blood-pressure, either in diagnosis or as a means of observing the progress of these conditions.

A detailed and most interesting account is given of the gross deformities of the pelvis, associated with general skeletal diseases and the impression is gained that osseous disease, such as tuberculosis and rickets, is a good deal more common in France, particularly as a cause of pelvic contraction, than in this country. In the management of contracted pelvis trial labour is not mentioned, though pubiotomy is favoured as a method of dealing with difficult labour due to this cause.

In the section dealing with forceps delivery, rotation by means of the midwifery forceps is advocated in cases where the occiput is not anterior, while manual rotation receives no description.

In post-partum haemorrhages hot douches and bimanual compression are favoured while ergotine and ergotinine are recommended as oxytocics—ergometrine and posterior pituitary extract are not included. Sulphonamides are not prescribed in the treatment of puerperal sepsis, though it is probable that this has been altered since this volume was written and that sulphonamides, and penicillin, which is now being produced in France, are used.

These criticisms serve to emphasize the differences in obstetrical practice between those in Britain and their French colleagues. The impression is gained that in France, midwifery is more conservative than in this country and that there is less tendency to resort to Caesarean section as a solution of obstetrical difficulties.

The book is admirably written and is notable for the clarity with which the author's views are expressed. The illustrations are excellent and numerous.

JOSEPHINE BARNES.

"Obstetrícia Prática." By L. A. HORTA BARBOSA, Reader in Clinical Obstetrics and Gynaecology in the Faculty of Medicine of the University of Brazil. Second edition; 518 pages with 341 illustrations. Price Cr\$. 250,000. Rio de Janeiro, Brazil: Edicoes Medicas da Editora Scientifica. 1945.

THIS book, the first treatise on midwifery from Latin-America reviewed by this journal, was awarded the Mme. Durocher Prize of the National Academy of Medicine of Brazil on its appearance in 1940. Mme. Durocher was the first female diplomate in obstetrics of the Faculty of Medicine

in Rio de Janeiro, in 1834, and the only woman ever elected to the membership of the Academy. She appears to have been a doctor who was able successfully to invade the province of the midwife in her adopted country (she was of French birth), and this book seems to have well deserved the award made in her name as it is intended for students and for those practitioners who must work without assistance in the remote rural areas of vast Brazil.

The author has been deeply influenced by his friend and mentor, Professor Fernando Magalhães, whose recent death has deprived South America of a great teacher. The book is dotted with phrases or whole paragraphs from Magalhães' admirable *Síntese Obstétrica*, and these have the quality of memorable simplicity that marks some of the utterances of Smellie, Harvey and Miles Phillips. The reviewer was led by Dr. Barbosa's many references to read *Síntese Obstétrica* and considers that it deserves wider examination in this country.

Dr. Barbosa's method is clinical and practical and limited to a description of signs, symptoms and treatment with the minimum of discussion of aetiology and laboratory diagnosis. He adds up for his readers the features of the clinical picture until an entity is produced and then applies a set, sound line of treatment. The very few methods of laboratory diagnosis are described in great practical detail so that the rural practitioner with the most rudimentary means may apply them.

The mechanism of labour is well and vividly described and illustrated. Adverse criticism may be here introduced, however. The wearing of a face mask by the accoucheur is not mentioned. It is possible that the climate of Rio de Janeiro does not favour the harbouring of pathogenic organisms in the upper respiratory tract but this is an omission that cannot be overlooked. The only antiseptic described is the somewhat outmoded oxyanurate of mercury (1:1000).

Too, drastic purgation is prescribed in pre-eclampsia; and tamponade of the vagina, repeated if necessary, is the advised treatment in placenta praevia, with Caesarean section as a second choice if tamponade fails, and the application of Willett's forceps is rather deprecated!

In the treatment of puerperal sepsis, too little mention is made of bacteriological diagnosis,

although this is probably deliberately done because of the hesitations of the readers for whom the book is intended, and it is a little odd in this epoch to hear of vaccine- and protein therapy and the intrauterine application of iodine cresote-glycerin as useful therapeutic measures.

In pyelitis of pregnancy a 6-8 g. daily dose of sulphathiazole is recommended with reduction of fluid intake!

But analgesia and anaesthesia in labour are well described and the note on local anaesthesia could not be bettered.

In the section on obstetric operations it is a pity that a book like this with its avowed range of readers should include an illustrated description of trachelotomy and vaginal hysterotomy, and this

is a criticism that may well be extended to similar textbooks of midwifery by other authors. The chapter on the obstetric forceps and breech delivery is very well done and the indications for Caesarean section wisely summarized in another quotation from Maghaliès as. "all dystocias which are impossible of solution by other means."

Resuscitation of the newborn assumes a more vigorous character than we are accustomed to practise in this country, stress being laid on the methods of artificial respiration now largely abandoned here.

In all, this is a well-written book, worthy of its purpose and the popularity it enjoys in the country of its origin.

MEAVE KENNY

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

D.R.C.O.G. EXAMINATION, OCTOBER 1945.

The following candidates satisfied the examiners for the DIPLOMA of the College:

Dirk Walter Bentinck.
Kenneth Joseph Robson Cuthbert.
Ada Inez Date.
Ann Donnelly.
William Donovan.
Mary Downey.
Mary Muriel Essex-Lapresti.
Margaret Fitzherbert.
Stanley Frederick Hans.
John Ormerod Harrison.
David Worsley James.
Philip Seukaran Jaikaran.
Gordon Trevor Johnson.
John Campbell Miller.
George William Mills.
Marjory Beatrice Morton.
David Charles Mundy.
Diana Joyce Myott.
James Raymond Owen.
Ada Violet Victoria Parkes.
Anthony John Partridge.
Stewart Sandeman Favell Pooley.
David Pryor Jones.
Otto Arnold Schmidt.
Victoria Marie Diana Nicoresti Shaw.
Laurence Spencer Stephens.
Charles Edward Riddiough Wood.
Geoffrey Worden.
John Harley Young.

INDEX TO CURRENT LITERATURE

In this Index an endeavour will be made, so far as conditions permit, to maintain an up-to-date record of all titles bearing on obstetrics and gynaecology and the infant. The classification aims at making immediately available for the reader the titles under the various headings. In the majority of instances the title is obtained from the original publication. Where this has been impossible, the title has been obtained from the abstracting journal shown in brackets. Reprints will be welcomed and should be sent to the Editor.

Any inquiries should be addressed to Miss D. F. Atkins, British Post-graduate Medical School, Ducane Road, London, W.12.

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ANATOMY

1. "The two main diameters at the brim of the female pelvis." C. Nicholson. *Journ. Anat.*, July 1945, LXXIX, 131-5.

PHYSIOLOGY

2. "Normal physiological douches." K. J. Karnaky. *Amer. Journ. Surg.*, July 1945, LXIX, 107-15.
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NORMAL

PREGNANCY

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Duration

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